ORGANIC CHEMISTRY for STEM MAJORS

Part 2 of 3

Workbook designed to accompany Organic Chemistry by David Klein, 4th ed

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10: RADICAL REACTIONS

MAIN IDEA

A radical is an atom or molecule with at least one unpaired electron. Radicals can react with other radicals by combining their unpaired electrons to form a covalent bond. More commonly, radicals react with covalent bonds to create new radicals.

OBJECTIVES

- Learn how radicals are formed
- Understand the types of reactions that can occur with a radical reactant

SKILLS TO MASTER

- Draw mechanisms for initiation, propagation, and termination reactions
- Draw products with correct stereochemistry for radical bromination and chlorination reactions

TERMINOLOGY

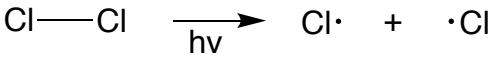
- Heterolytic cleavage
- Homolytic cleavage
- Initiation
- Propagation
- Regioselective
- Termination

1: COMMON PATTERNS IN RADICAL MECHANISMS

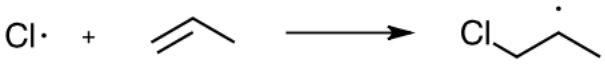
Used to show the motion of 1 electron

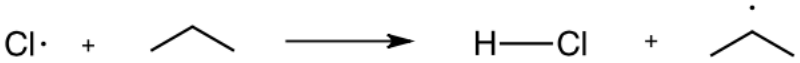
Used to show the motion of 2 electrons

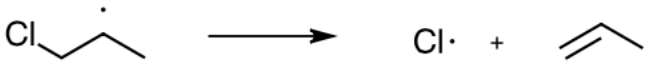
1. ***Initiation*** is a reaction that creates radicals from non-radicals. Draw the curved arrows for the following initiation reaction. Make sure you are using "fishhook" curved arrows to show the movement of a single electron.



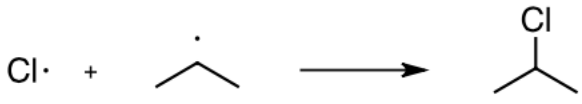
2. ***Propagation*** is a reaction that creates new radicals. It has at least one radical reactant and at least one radical product. There are many different types of propagation reactions, including adding a radial to a pi bond, using a radical to abstract a hydrogen, or elimination. Draw the curved arrows for the following propagation reactions.







3. Termination is a reaction that combines two radicals to create a non-radical. Draw the curved arrows for the following termination reaction.



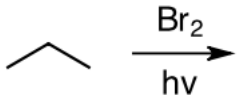
4. The chlorination of methane is one of the most studied radical reactions. This reaction is initiated when light (or heat) interacts with Cl_2 to form chlorine radicals. Draw this step.

5. Next, a chlorine radical abstracts a hydrogen from methane. The products are a methyl radical and HCl. Draw this step.

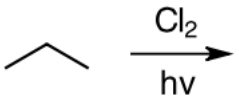
6. After the methyl radical is formed, there are many possible reactions. Draw the methyl radical reacting with a chlorine radical in a termination step to produce CH_3Cl.

2: REGIOSELECTIVITY AND STEREOCHEMISTRY OF HALOGENATION

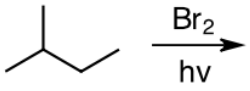
1. The bromine radical is relatively stable, and it only proceeds via the most stable intermediate(s). For this reason, radical bromination is *regioselective.* The following radical reaction produces only one product. Determine the most stable carbon radical intermediate that can be formed from propane. Use this to predict the brominated product of the reaction, and draw its structure.



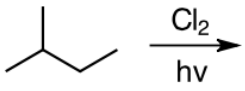
2. The chlorine radical is unstable. Reactions involving the chlorine radical will proceed without selectivity. The following radical reaction produces two products. Determine both possible carbon radial intermediates that can be formed from propane. Use them to predict both chlorinated products of the reaction, and draw their structures. Identify the major product.



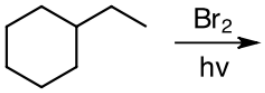
3. Draw the structure of the one product of the following reaction.

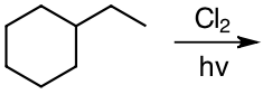


4. Draw the structures of the 6 products of the following reaction and identify the major product. (Hint: There are 4 constitutional isomers and 2 pairs of stereoisomers.)



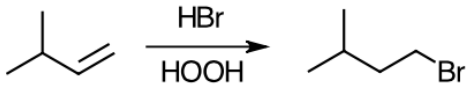
5. Draw all products for the following reactions, and identify the major product of each reaction. For the chlorination reaction, there are fourteen possible products.





3: ANTI-MARKOVNIKOV ADDITION OF HBR

Follow the steps below to propose a mechanism for the anti-maokovnikov addition of HBr to an alkene.



1. Begin by drawing the homolytic cleavage of peroxide to form two hydroxyl radicals.

2. Next, draw a hydroxyl radical reacting with HBr to produce a bromine radical.

3. Next, draw a bromine radical reacting with the alkene to form a brominated alkyl radical.

4. Last, propose a termination or propagation reaction that will produce the desired final product.

11: SYNTHESIS

MAIN IDEA

In order to make significant structural changes to molecules, organic chemists often need to combine a variety of reactions in a multi-step synthetic pathway. When developing multi-step syntheses, start by making sure the reactant molecule has a functional group. If the reaction is starting with an alkane, it should be halogenated using a free-radical halogenation reaction. Next, ignore functional groups and compare the carbon skeletons of the reactants and products. There are a limited number of reactions that change the carbon skeleton of a molecule. If a carbon skeleton transformation is necessary, it should be identified as soon as possible. Last, remove any unwanted functional groups and add any desired functional groups. Sometimes this process can be simultaneous (in a substitution reaction, for example). In other instances, this needs to be done through elimination and addition.

OBJECTIVES

- Learn how to combine halogenation, substitution, elimination, and addition reactions to perform significant structural modifications to organic molecules

SKILLS TO MASTER

- Propose multi-step reactions, including retrosynthetic pathways, to convert a reactant to a desired product

4: SYNTHESIS

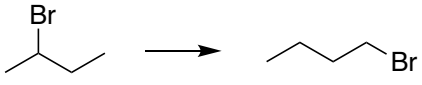
Show how to perform each of the following conversions. To approach these problems, use the following strategy:

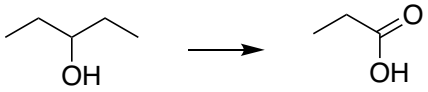
1: Are you starting with an alkane? If so, halogenate it via free radical bromination.

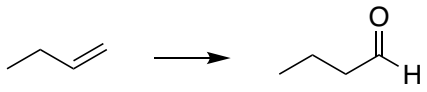
2: Do you need to change the carbon skeleton? If so, which reaction do you need to use?

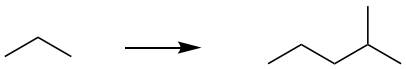
3: Which functional group needs to be removed from the molecule? Can it be removed as it is, or will it need to be modified before it can be removed?

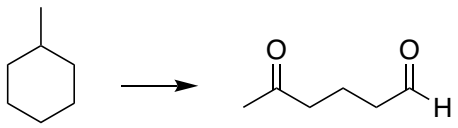
4: Which functional group needs to be added to the molecule? What reactions will add that functional group? If you need to do an addition reaction, do you have a double or triple bond present? If not, how can you get a double or triple bond onto the molecule in the right location? If you need to do a substitution reaction, do you have a good leaving group in the right spot?











12: ALCOHOLS AND PHENOLS

MAIN IDEA

Alcohols and phenols are molecules that contain an isolated -OH functional group. As we have seen in the past, the alcohol functional group is relatively easy to convert to another functional group in a substitution reaction. It can also be removed from the molecule in an elimination reaction. In this chapter, we will learn how to oxidize the alcohol functional group, which ultimately converts the carbon-oxygen single bond into a carbon-oxygen double bond. We will also learn a variety of reactions used to synthesize alcohols, including one reaction which allows us to also increase the length of the carbon skeleton of the molecule.

OBJECTIVES

- Learn how to name alcohols and diols
- Understand the difference between an alcohol and a phenol
- Understand that alcohols are weakly acidic and can be deprotonated to make strong bases
- Understand oxidation and reduction as it applies to organic molecules
- Learn how Grignard reagents are formed and used to synthesize alcohols
- Learn how to convert alcohols to alkyl halides

SKILLS TO MASTER

- Name alcohols and diols using IUPAC rules
- Predict the relative stability of alkoxide ions
- Draw the mechanisms for the following reduction reactions:
    - Conversion of ketone to alcohol
    - Conversion of aldehyde to alcohol
    - Conversion of carboxylic acid to alcohol
    - Conversion of ester to alcohol

- Draw the mechanisms to show how Grignard reagents react with the following functional groups:
    - Ketone
    - Aldehyde
    - Ester
- Identify the correct reagents needed to form a Grignard reagent and use it to synthesize a desired alcohol
- Identify the correct reagents needed to perform the following oxidations:
    - Primary alcohols to aldehydes and carboxylic acids
    - Secondary alcohols to ketones
- Identify the correct reagents needed to perform the following conversions:
    - Primary, secondary, and tertiary alcohols to alkyl bromides
    - Primary and secondary alcohols to alkyl chlorides

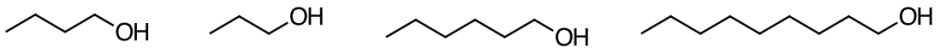
TERMINOLOGY

- Alcohol
- Alkoxide
- Diol
- Grignard reagent
- Oxidation
- Phenol
- Protecting group
- Reduction

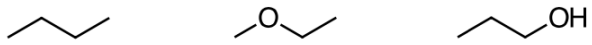
5: STRUCTURE AND PROPERTIES OF ALCOHOLS

1. Alcohols with more than 8 carbons are not soluble in water. Propose an explanation for this observation.

2. Rank the following alcohols in order of increasing solubility in water.



3. Explain the following trend in boiling points.

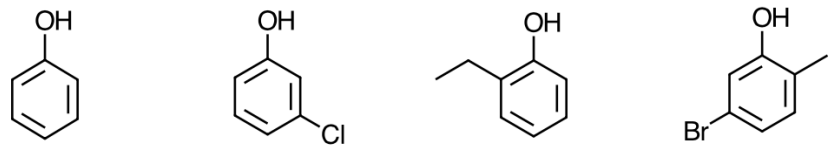


MW = 58
bp = -1 C

MW = 60
bp = 7 C

MW = 60
bp = 97 C

4. Phenols are benzene rings with an -OH group. As a rule, the -OH group is always located on C#1. Look at the following examples and propose IUPAC names for the last two phenols.



phenol

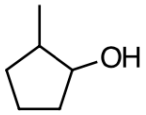
3-chlorophenol

5. To name an alcohol by IUPAC rules:

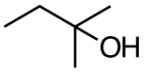
- Find the longest carbon chain containing the -OH group
- Give the -OH group the lowest possible number
- Follow all IUPAC rules regarding stereochemistry and substituents
- Replace the “-e” ending of the parent chain with “-ol”

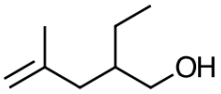
Look at the following examples and the provide names for the remaining alcohols.

2-propanol
propan-2-ol



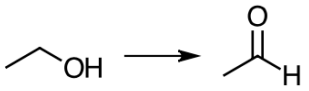
2-methylcyclopentanol

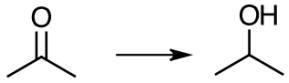


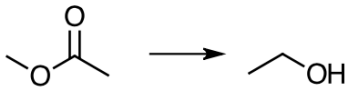


6: PREPARATION OF ALCOHOLS VIA REDUCTION

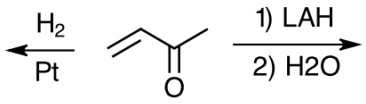
1. Classify the following reactions as oxidation or reduction.



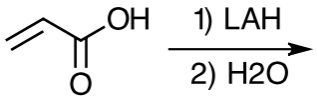




2. Predict the products of the following reactions.



3. In addition to reducing aldehydes and ketones, LAH can also be used to reduce carboxylic acids and esters. Propose a mechanism for the following reaction, based on the mechanism for $NaBH_4$ reacting with a ketone. *Hints: Attack with a hydride ion, form an aldehyde, attack the aldehyde with another hydride ion, and use water to "clean up" your product. Hydroxide will be a leaving group in this mechanism, and this is only possible because the hydride ion is a stronger base than hydroxide.*

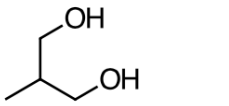


7: PREPARATION OF DIOLS

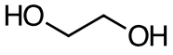
1. To name a diol by IUPAC rules:

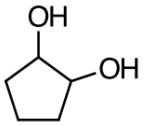
   - Find the longest carbon chain containing both -OH groups
   - Give the -OH groups the lowest possible numbers
   - Follow all IUPAC rules regarding stereochemistry and substituents
   - Keep the “-e” ending of the parent chain and add “-diol”

Look at the following example and the provide names for the remaining alcohols.

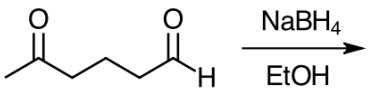


2-methyl-1,3-propanediol



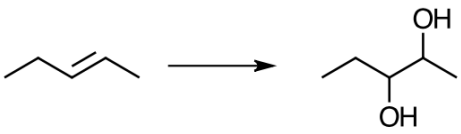


2. Diols can be prepared by reducing dicarbonyls. Predict the product of the following reaction.



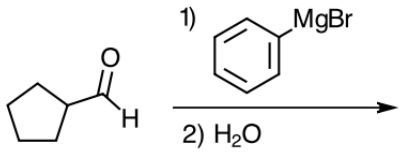
3. Identify two other sets of reagents that could be used for the reaction in problem 2.

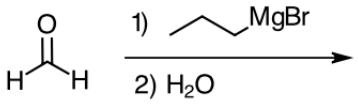
4. Diols can be prepared from an alkene. Identify reagents needed to perform the following conversion. (There is more than one set of reagents that can be used.)

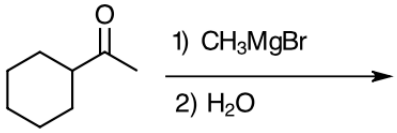


8: PREPARATION OF ALCOHOLS VIA GRIGNARD REACTIONS

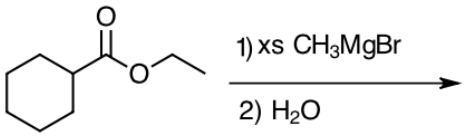
1. Predict the products of the following reactions.



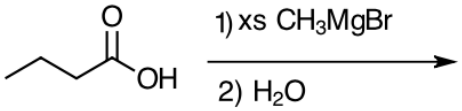




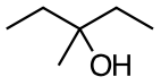
2. Grignards also react with esters. This reaction requires excess Grignard reagent. Propose a mechanism for the following reaction. *Hints: Attack with a Grignard, form an anion intermediate, form a ketone by kicking off an alkoxide leaving group, attack with another Grignard and proceed as usual. Alkoxide can be a leaving group in this mechanism because the Grignard reagent is a stronger base than an alkoxide.*

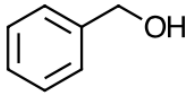


3. Grignards also react with carboxylic acids, but not in the usual way. Grignards are very strong bases, so they will react with a carboxylic acid in a simple acid-base reaction. Draw a mechanism for the following reaction. *Hint: The Grignard reagent will not attack a carbon atom in this mechanism.*



4. Show how to make the following alcohols via a Grignard reaction. Include formation of the Grignard reagent from an alkyl halide.

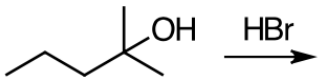




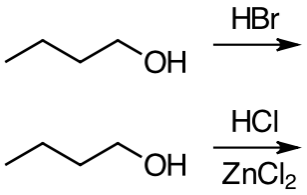
9: REACTIONS OF ALCOHOLS: SUBSTITUTION AND ELIMINATION

Predict the products of the following reactions of alcohols.

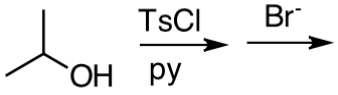
1. Secondary and tertiary alcohols can undergo S_N1 reactions. Don't forget about rearrangement of the carbocation intermediate.

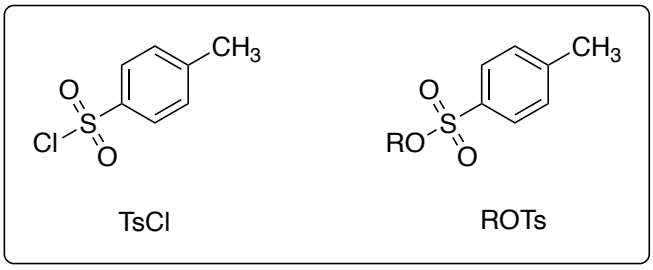


2. Primary alcohols can undergo an S_N2 reaction with HX. When using HCl, a $ZnCl_2$ catalyst is necessary.

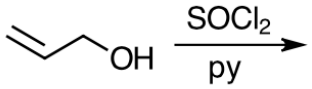


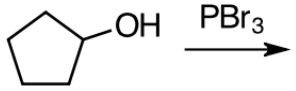
3. Primary and secondary alcohols can undergo any S_N2 reaction if the OH group is covered to a better leaving group using tosyl chloride, TsCl. The conversion of -OH to -OTs is performed in pyridine ("py"), a solvent.



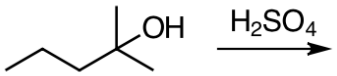


4. Primary and secondary alcohols can undergo an S_N2 reaction with $SOCl_2$ or PBr_3. These reactions form an alkyl halide.

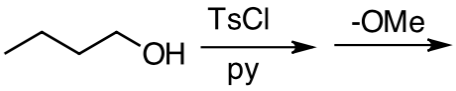




5. Secondary and tertiary alcohols can undergo an E1 reaction. Don't forget about rearrangement, and look for all possible alkene products.

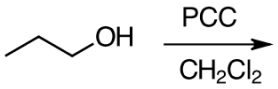


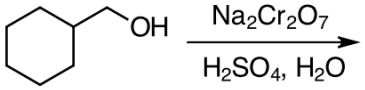
6. Primary and secondary alcohols can undergo an E2 reaction if they are first converted to -OTs.

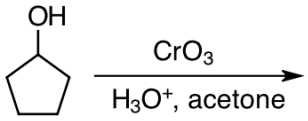


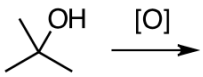
10: REACTIONS OF ALCOHOLS: OXIDATION

Predict the products of the following reactions.









13: ETHERS AND EPOXIDES

MAIN IDEA

Ethers are molecules that contain an oxygen atom in the middle of a carbon chain. They can be either straight chain or cyclic, with the oxygen atom being one of the members of the ring. Most ethers are relatively non-reactive, which makes them valuable solvents in the lab. Many reactions are performed in an ether solvent without concern that the ether will interfere with the desired chemical reaction. Ethers can be synthesized via nucleophilic substitution or via addition to an alkene.

OBJECTIVES

- Learn the IUPAC system for naming ethers
- Understand the common nomenclature of ethers
- Understand the difference between an ether and an epoxide
- Learn how to synthesize both ethers and epoxides
- Learn how to convert ethers to alkyl halides
- Learn how to open the ring of an epoxide

SKILLS TO MASTER

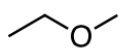
- Name ethers using both IUPAC rules and common nomenclature
- Identify the correct reagents needed to perform the following conversions:
    - Alcohols, phenols, and/or alkyl halides to ethers via the Williamson ether synthesis
    - Alkenes to ethers via alkoxymercuration-demercuration
    - Alkenes and halohydrins to epoxides
- Draw the mechanisms for the following reactions:
    - Acidic cleavage of an ether
    - Epoxide ring-opening under acidic or basic conditions

TERMINOLOGY

- Epoxide
- Ether
- Halohydrin

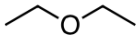
11: NOMENCLATURE OF ETHERS

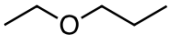
1. Common nomenclature can only be used on ethers with small and simple alkyl groups. To use common nomenclature, name each alkyl group in alphabetical order and then add "ether" at the end - three separate words. If the two alkyl groups are the same, use the prefix "di-" and "ether" - two separate words. View the examples above, and then give common names to the ethers below.



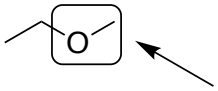
ethyl methyl ether

dimethyl ether



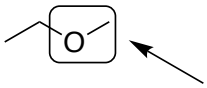


2. IUPAC nomenclature does not recognize ethers as afunctional group. Rather, the oxygen and one of the ether's alkyl groups are named as a substituent on the other alkyl group. To name an ether using IUPAC rules:



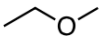
The OCH_3 will be named as a substituent on the two-carbon chain

- Identify the ether's smallest alkyl group
- Number and name the larger alkyl group following IUPAC rules
- Name the ether's oxygen and small alkyl group as an "alkoxy" substituent
  - *Alkoxy substituent's names are based on the name of their relative alcohol. Imagine the alkoxy substituent as an alcohol molecule. Name this alcohol molecule. Then, drop the "-anol" from the end of the alcohol's name and replace it with "-oxy". View the explanation to the right.*

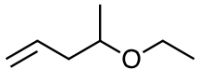


The OCH_3 is based on CH_3OH. CH_3OH is methanol, and CH_3O as a substituent is methoxy.

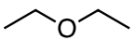
View the examples below, and the give IUPAC names to the other ethers.

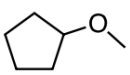


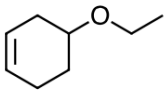
1-methoxyethane



4-ethoxy-1-pentene
4-ethoxypent-1-ene

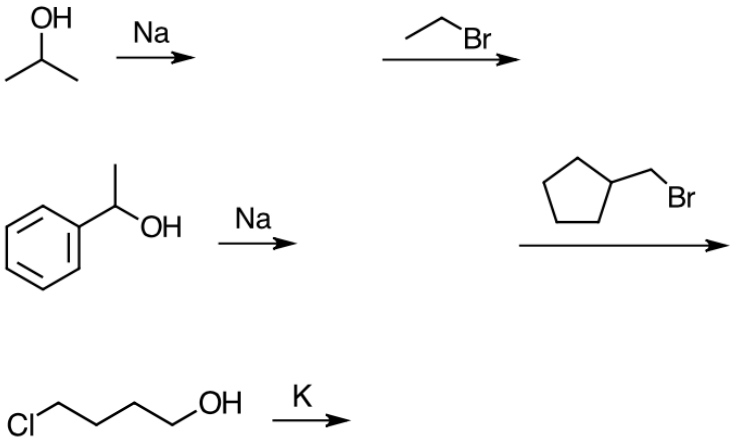




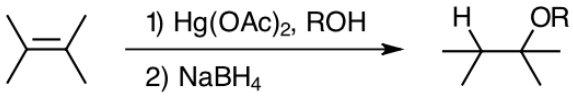


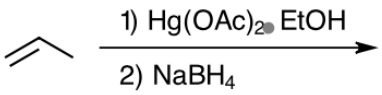
12: PREPARATION OF ETHERS

1. The Williamson Ether Synthesis is an SN2 reaction where the nucleophile is an alkoxide ion. View the generic reaction to the right and then predict the products for the reactions below. *Note: You can use either Na or Li or K in place of NaH.*



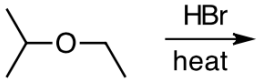
2. Alkoxymercuration-demercuration is similar to oxymercuration-demercuration. Instead of using water to add H-OH across a double bond, it uses alcohol to add RO-H across a double bond. View the generic reaction to the right and then predict the product of reaction below.

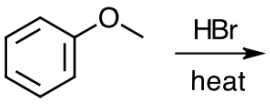


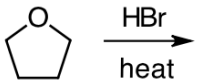


13: REACTIONS OF ETHERS

Draw the products of the following reactions.

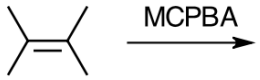


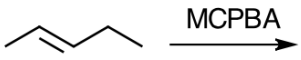




14: PREPARATION OF EPOXIDES

1. Predict the products of the following alkene addition reactions. Make sure to include correct stereochemistry.

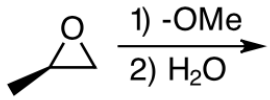




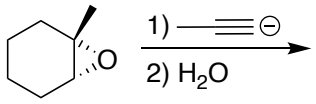
2. Predict the products of the following two-step processes. The first step is an alkene addition reaction, and the second step is the Williamson Ether Synthesis. Make sure to include correct stereochemistry.

15: RING-OPENING REACTIONS OF EPOXIDES

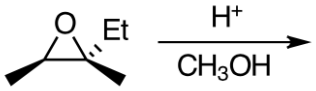
1. When an epoxide is reacted with a base, the base always attacks the epoxide's carbon with the least steric hinderance. Draw the mechanism for the following reaction.

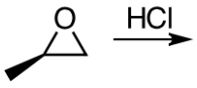


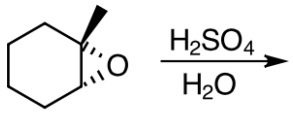
2. The mechanism for the basic ring opening of an epoxide is similar to an S_N2 reaction. The carbon that is attacked will undergo inversion of configuration. (The other carbon does not change stereochemistry because it is not attacked.) Draw the mechanism for the following reaction, showing the correct stereochemistry of the product.



3. When an epoxide is reacted with an acid, the reaction begins with the acid protonating the oxygen of the epoxide. Then, the nucleophile attacks the epoxide at a tertiary carbon. If there is no tertiary carbon, the nucleophile attacks a primary carbon. Stereochemistry always inverts. Draw the mechanisms for the following reactions, and show the correct stereochemistry of the products.







16: SYNTHESIS STRATEGIES

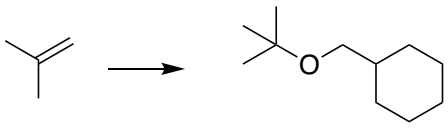
Show how to perform each of the following conversions. To approach these problems, use the following strategy:

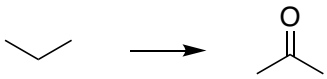
1: Are you starting with an alkane? If so, halogenate it via free radical bromination.

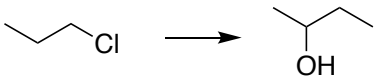
2: Do you need to change the carbon skeleton? If so, which reaction do you need to use?

3: Which functional group needs to be removed from the molecule? Can it be removed as it is, or will it need to be modified before it can be removed?

4: Which functional group needs to be added to the molecule? What reactions will add that functional group?







14: INFRARED SPECTROSCOPY (IR) AND MASS SPECTROMETRY (MS)

MAIN IDEA

Organic molecules can be evaluated using infrared spectroscopy (IR) and mass spectrometry (MS). Infrared spectroscopy uses infrared radiation to test for the presence of certain types of bonds in a molecule. It provides information about whether or not a molecule contains double or triple bonds, and can also provide information about whether or not a molecule contains oxygen or nitrogen. Mass spectrometry provides information about the molecular weight of a molecule, as well as the presence of bromine or chlorine atoms.

OBJECTIVES

- Understand what types of bonds appear in an IR spectrum and learn the general location of peaks associated with different types of bonds
- Understand what causes the different peaks in an mass spectrum
- Learn how to identify bromine, chlorine, and nitrogen based on MS data
- Learn how to identify oxygen based on IR data
- Understand the Rule of 13
- Understand HDI and learn how to use it to propose potential constitutional isomers for a molecular formula

SKILLS TO MASTER

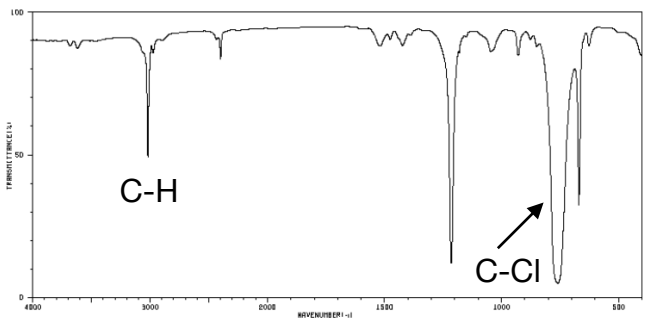
- Identify the general location of IR peaks associated with alkenes, alkynes, nitriles, carbonyls, alcohols, and amines
- Use MS data to determine the molecular weight of a molecule
- Use MS data to determine if a molecule has bromine atoms, chlorine atoms, or an odd number of nitrogen atoms
- Use the Rule of 13, molecular weight, and information about heteroatoms to predict the formula of a molecule
- Use HDI to predict if a molecule contains double bonds, triple bonds, or rings

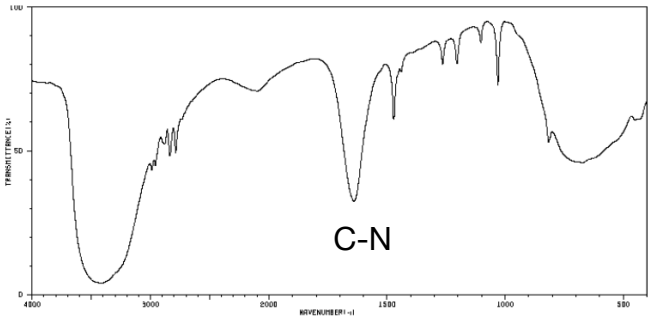
TERMINOLOGY

- Fingerprint region
- Heteroatom
- Hydrogen deficiency index (HDI)
- M+2
- Molecular ion
- Nitrogen rule
- Rule of 13
- Wavenumber

17: WAVENUMBER

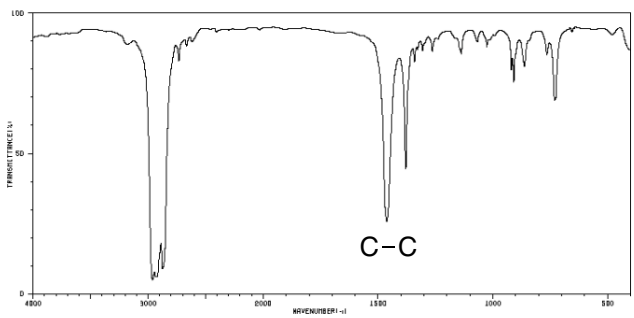
Compare the locations of the C-H, C-Cl, and C-N peaks in the IR spectra of $CHCl_3$ (left) and $(CH_3)_3N$ (right).

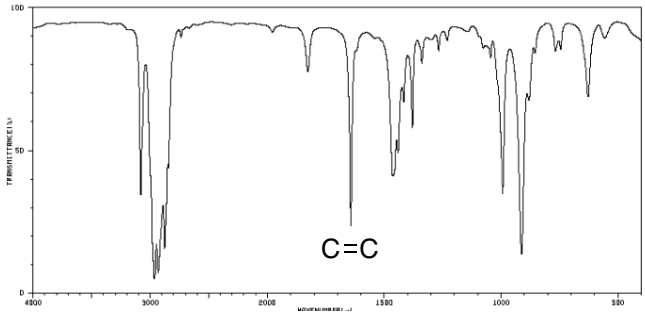


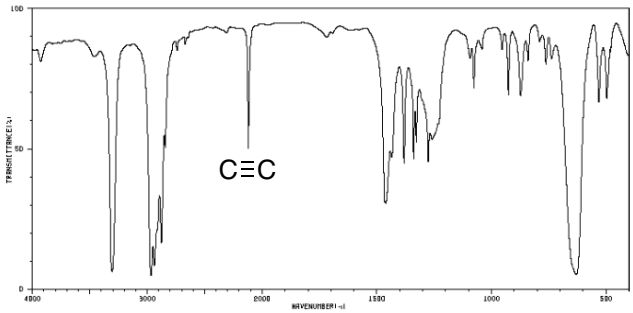


As the atoms in a bond get heavier (H vs. N vs. Cl), how does this affect the location of their peaks in an IR spectrum?

Compare the locations of the single, double, and triple carbon-carbon bonds in the IR spectra of pentane, 1-pentene, and 1-pentyne.





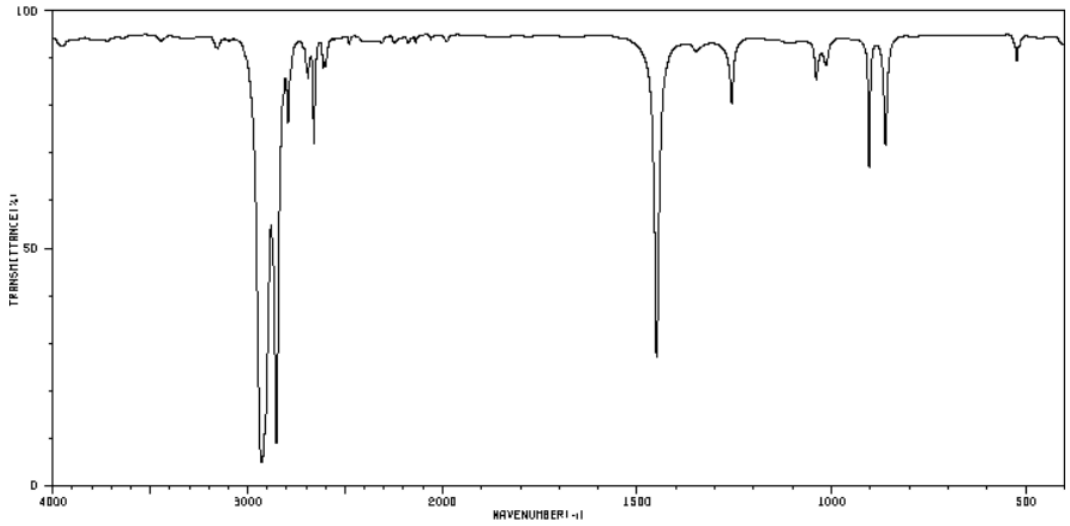


As bonds get stronger (single vs. double vs. triple), how does this affect the location of their peaks in an IR spectrum?

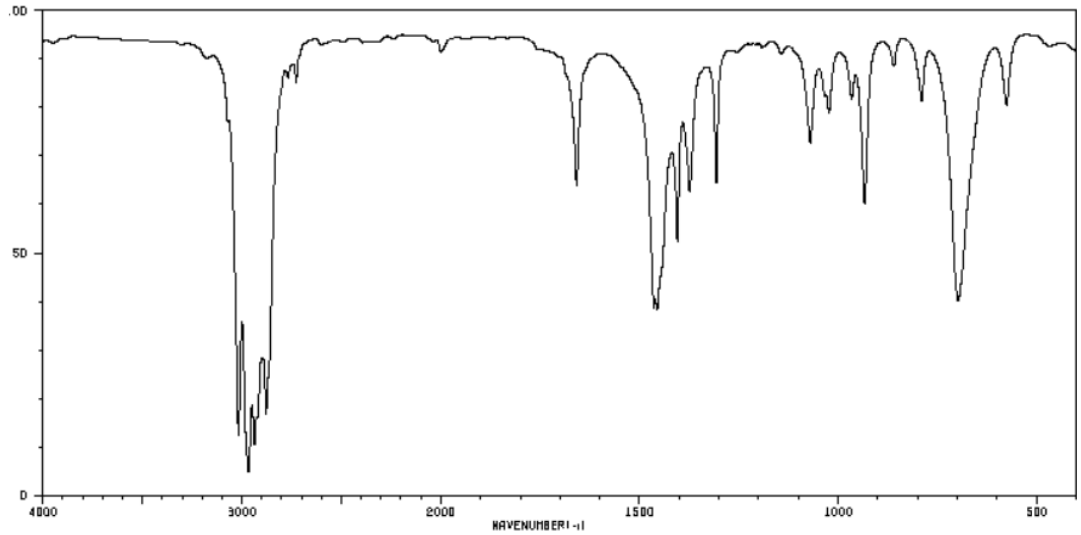
18: BASIC IR ANALYSIS

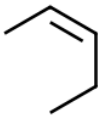
In most instances, an IR spectrum will not be used to determine the complete structure of an unknown molecule. Instead, chemists will use IR along with other types of spectroscopy to determine the structure of an unknown molecule. In this method of combined spectral analysis, IR is only used to identify which functional groups are present in a molecule. In this worksheet, you will practice identifying functional groups in IR spectra, without attempting to analyze all the peaks. It is common for students to want to analyze and understand every peak in an IR spectrum. Try to avoid this practice, as it is generally unnecessary and not a good use of time.

1. Locate the C-H peak in the spectrum of cyclohexane.

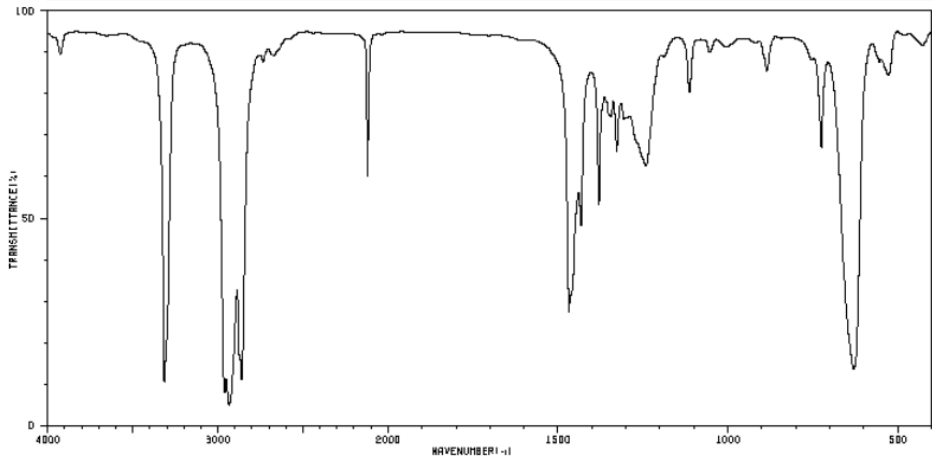


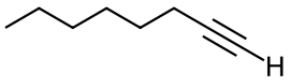
2. Locate the C-H and C=C peaks in the spectrum of *cis*-2-pentene.



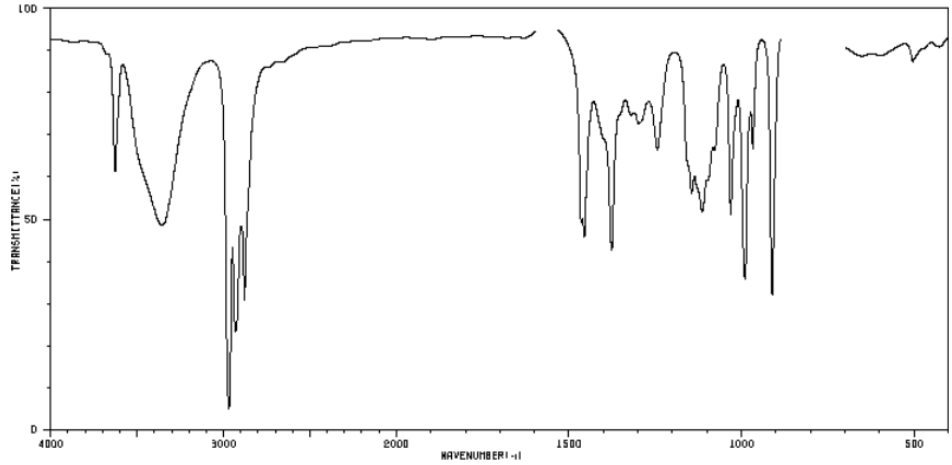


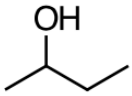
3. Locate the C-H, C≡C, and C≡C-H peaks in the spectrum of 1-octyne.



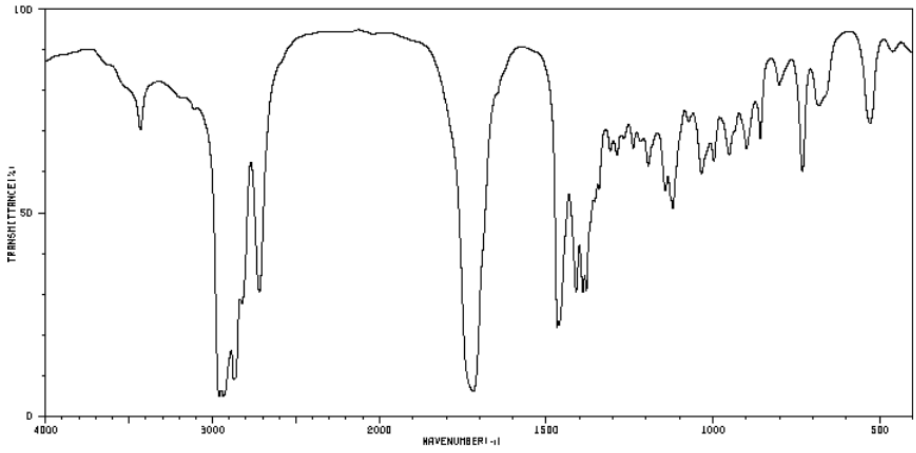


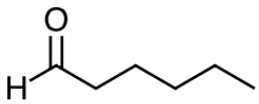
4. Locate the C-H and O-H peaks in the spectrum of 2-butanol.



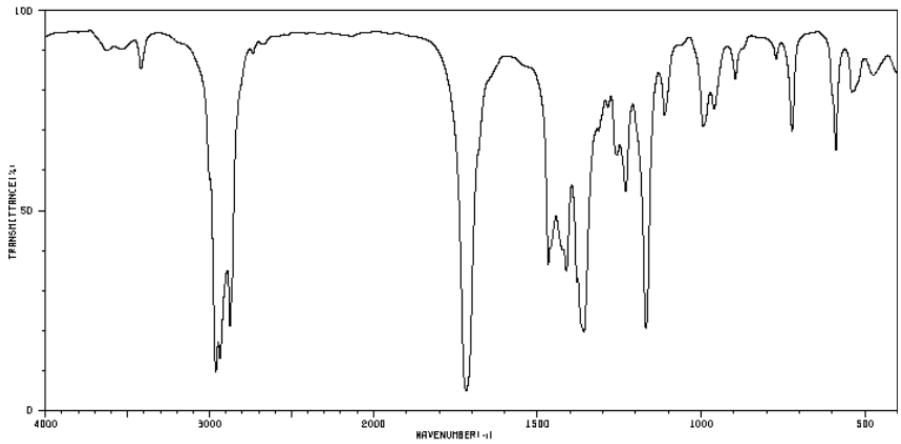


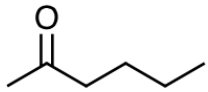
5. Locate the C-H, C=O, and H-C=O peaks in the spectrum of hexanal.



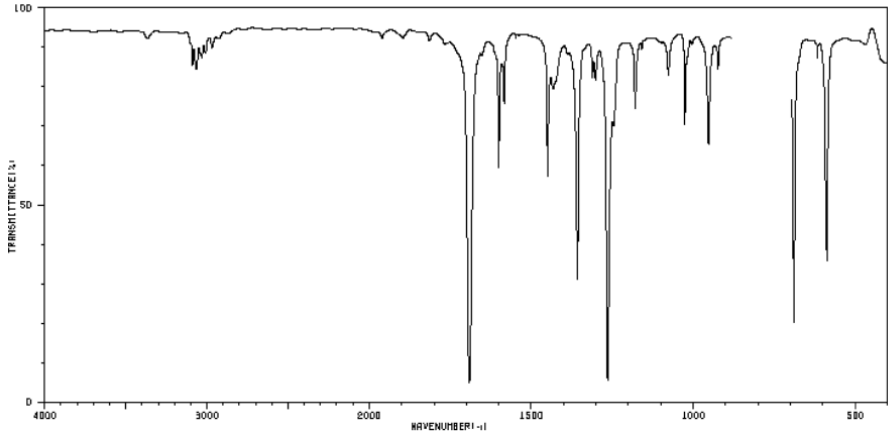


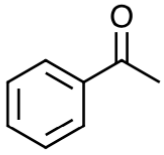
6. Locate the two important peaks in the spectrum of 2-hexanone.



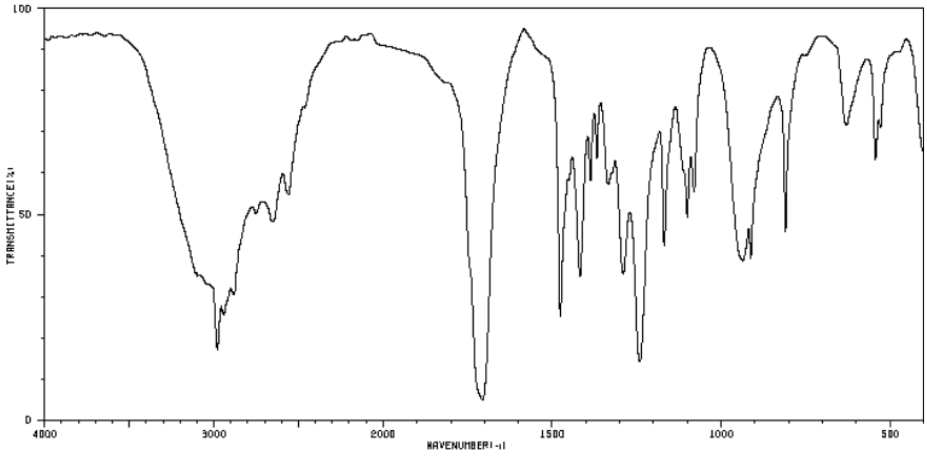


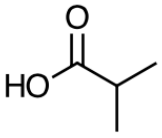
7. Compare the spectrum of acetophenone (below) to that of 2-hexanone (above). Identify the one important peak for acetophenone. Identify the absence of a peak that is normally observed. (This absence is a characteristic of the benzene ring



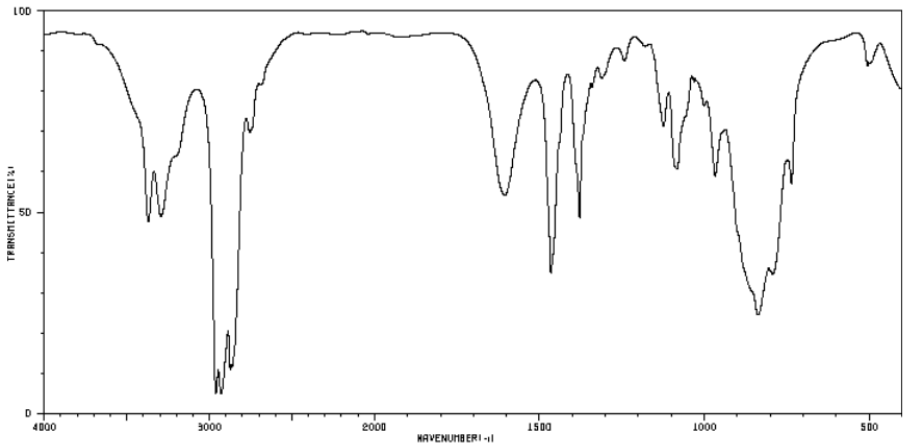


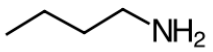
8. Locate the C=O and O-H peaks in the spectrum of 2-methylpropanoic acid. Why aren't the normal C-H peaks visible?



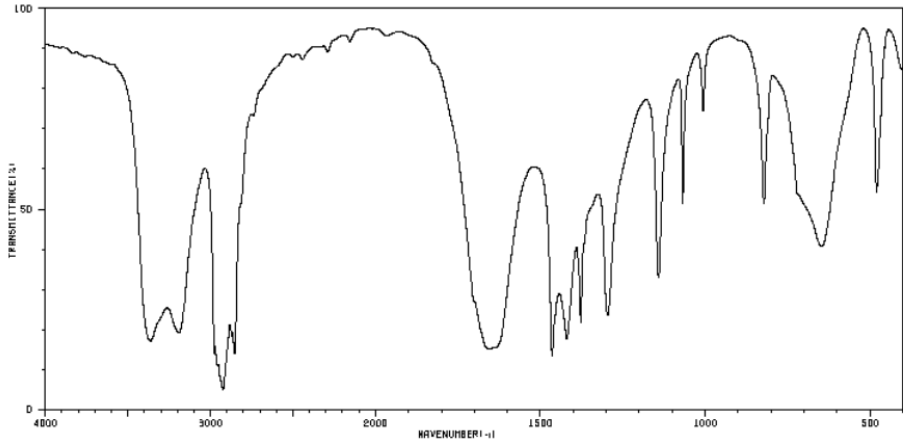


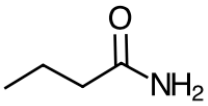
9. Locate the C-H and two N-H peaks in butylamine.



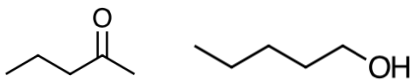


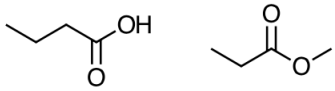
10. Locate the four important peaks in propionamide.

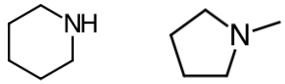




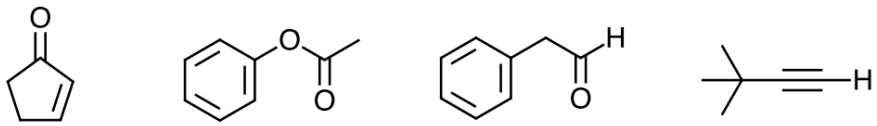
11. For each pair of compounds, explain how you would use IR to distinguish the two molecules.

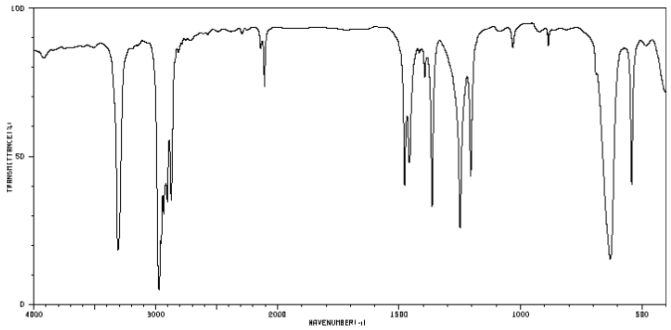


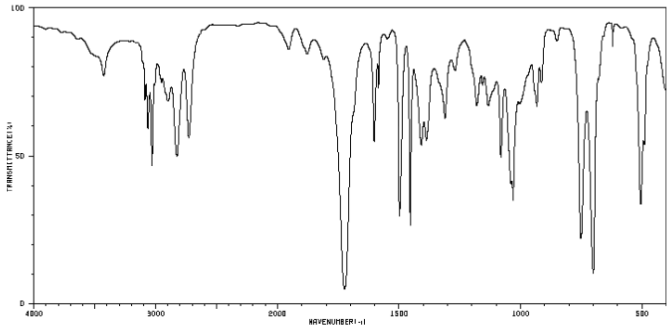


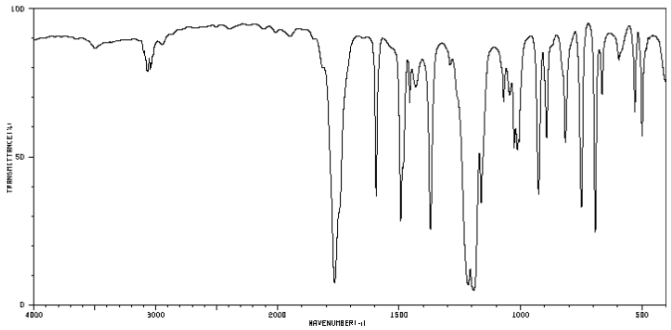


12. Three IR spectra are shown, corresponding to three of the four provided molecules. Match each spectrum to the correct molecule. One molecule will not be matched with a spectrum.

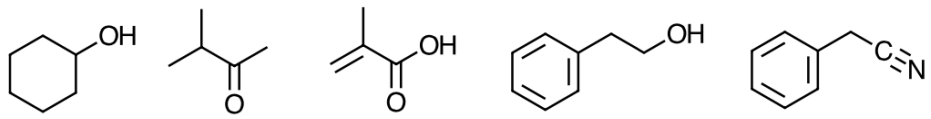


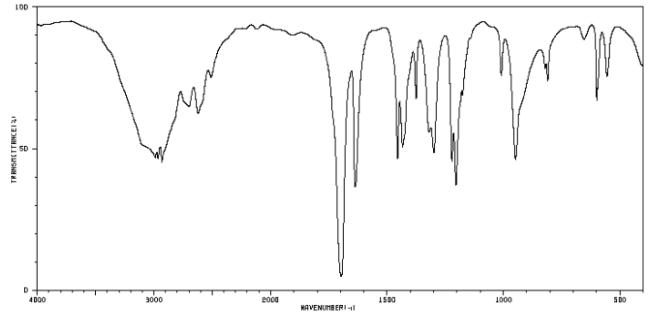


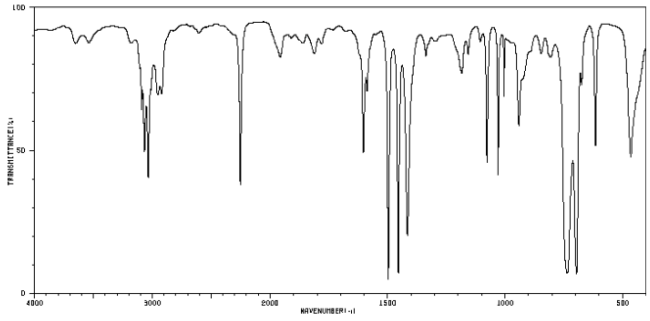


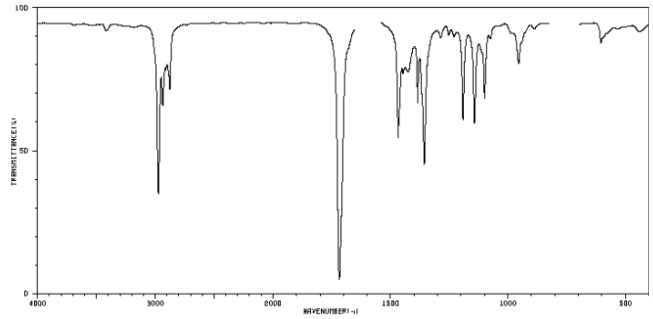


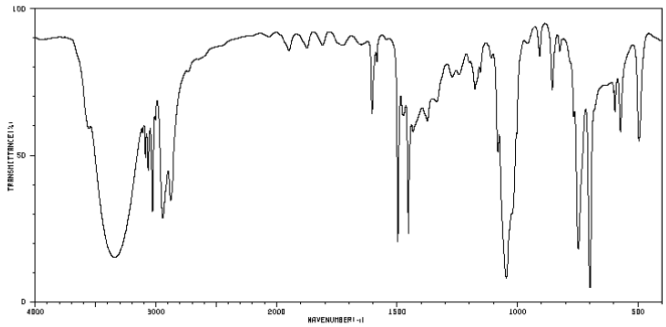
13. Four IR spectra are shown, corresponding to four of the five provided molecules. Match each spectrum to the correct molecule. One molecule will not be matched with a spectrum.







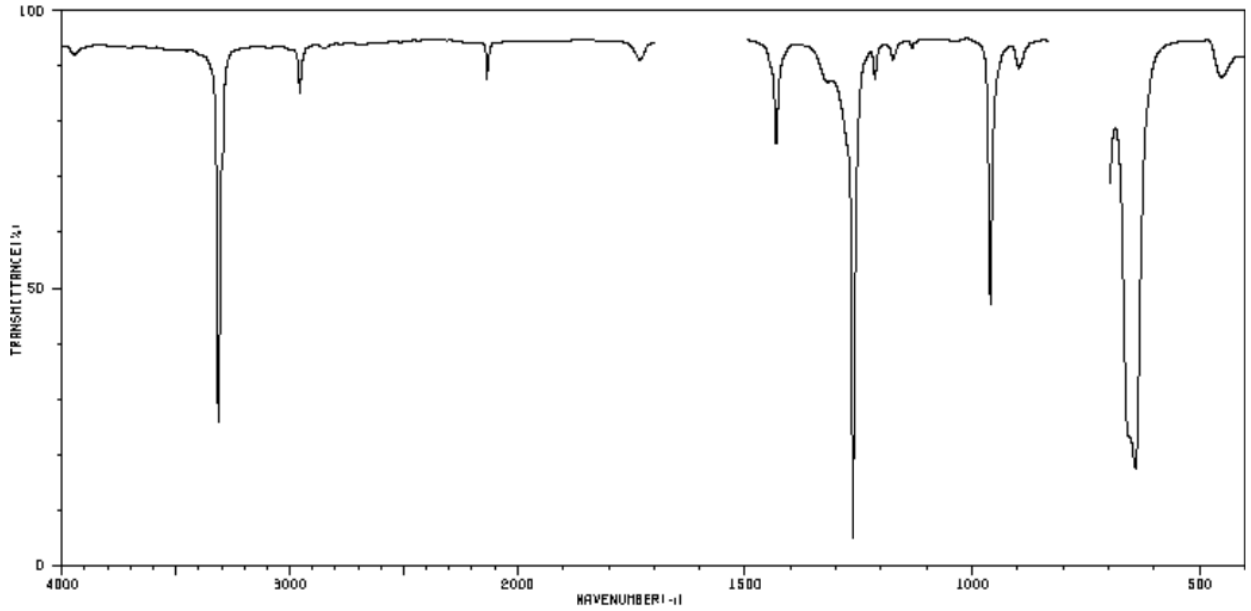




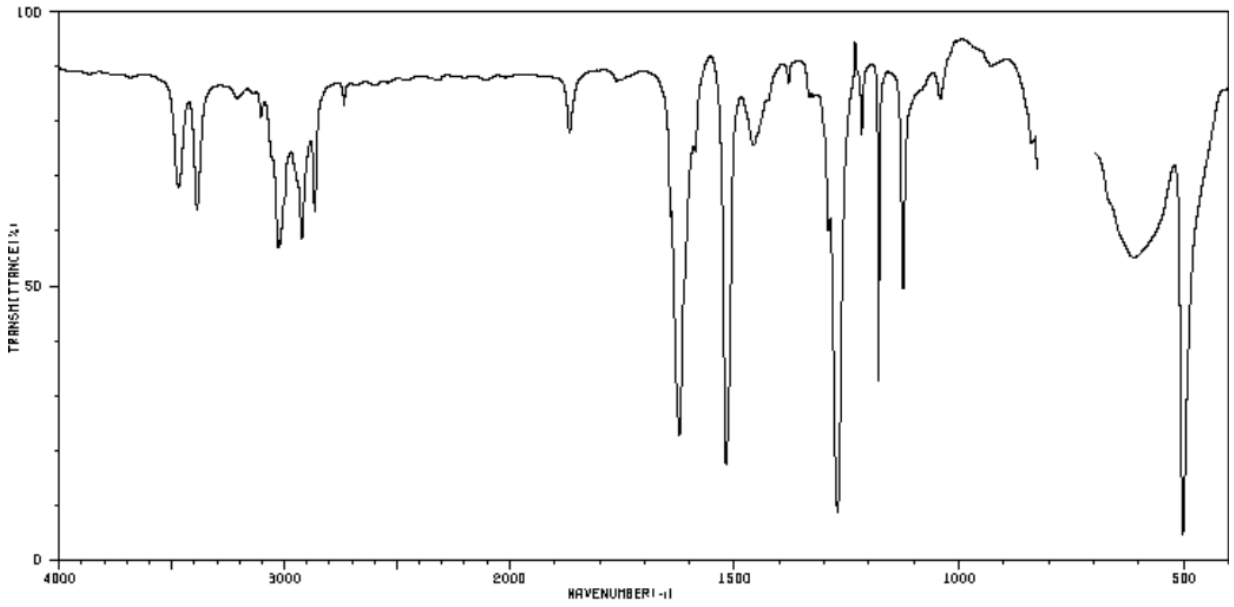
19: ADVANCED IR ANALYSIS

Propose a structure that is consistent with each IR spectrum. Molecular formulas are provided. There may be more than one reasonable answer for each spectrum.

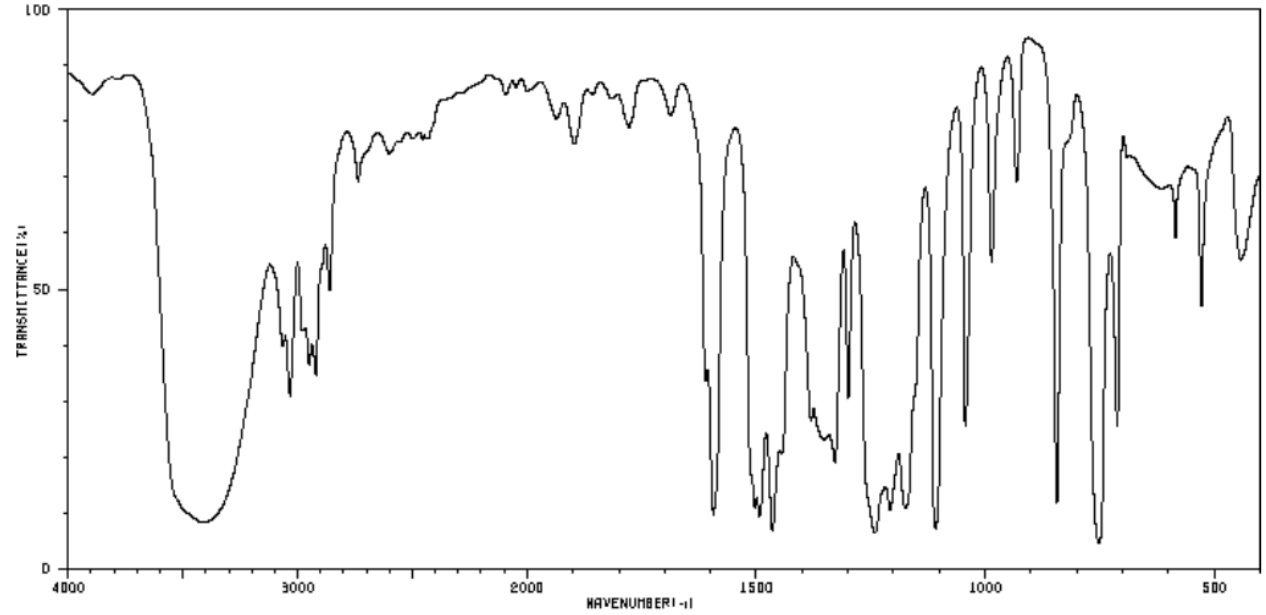
1. C_3H_3Cl



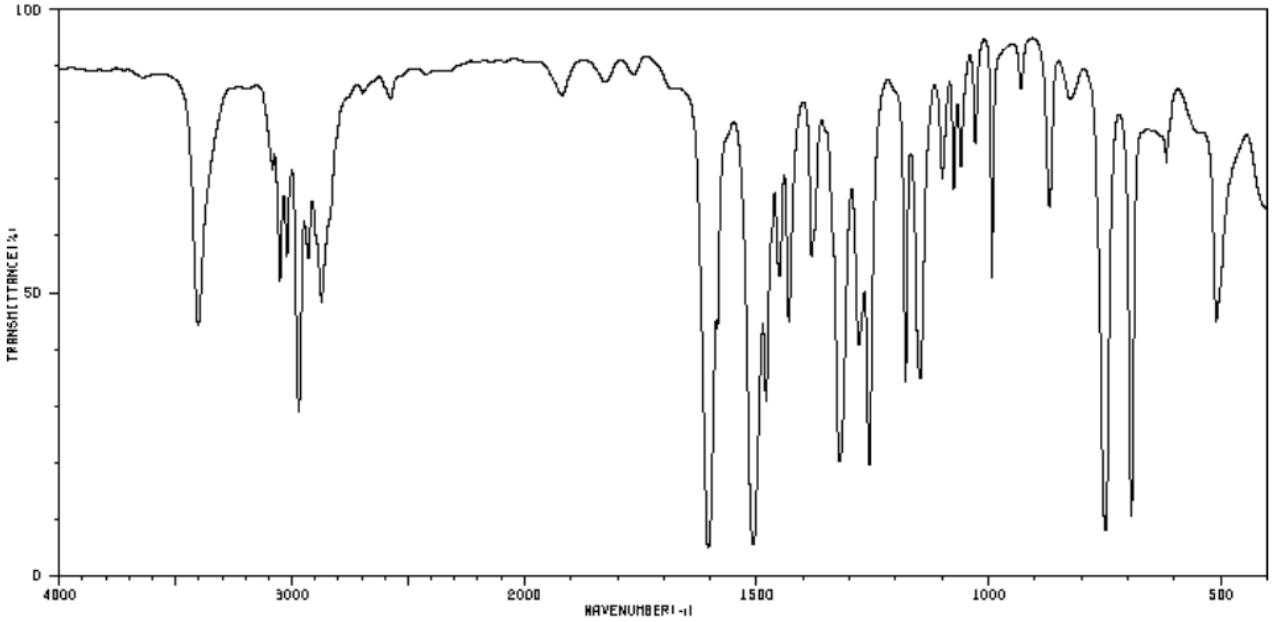
2. C_7H_9N



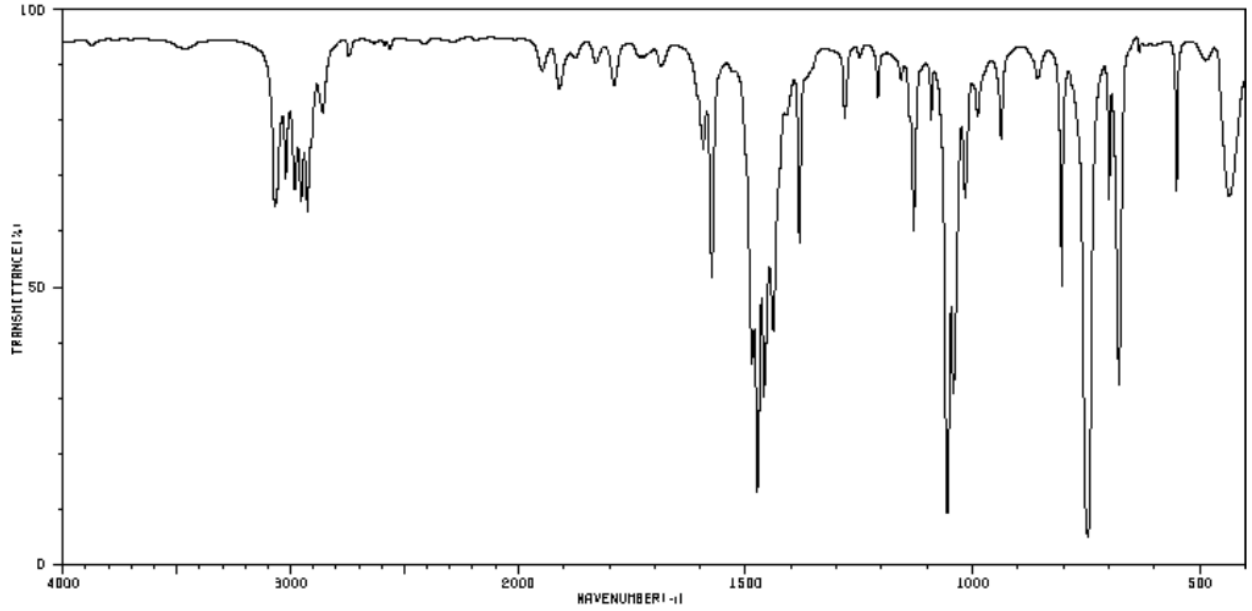
3. C_7H_8O



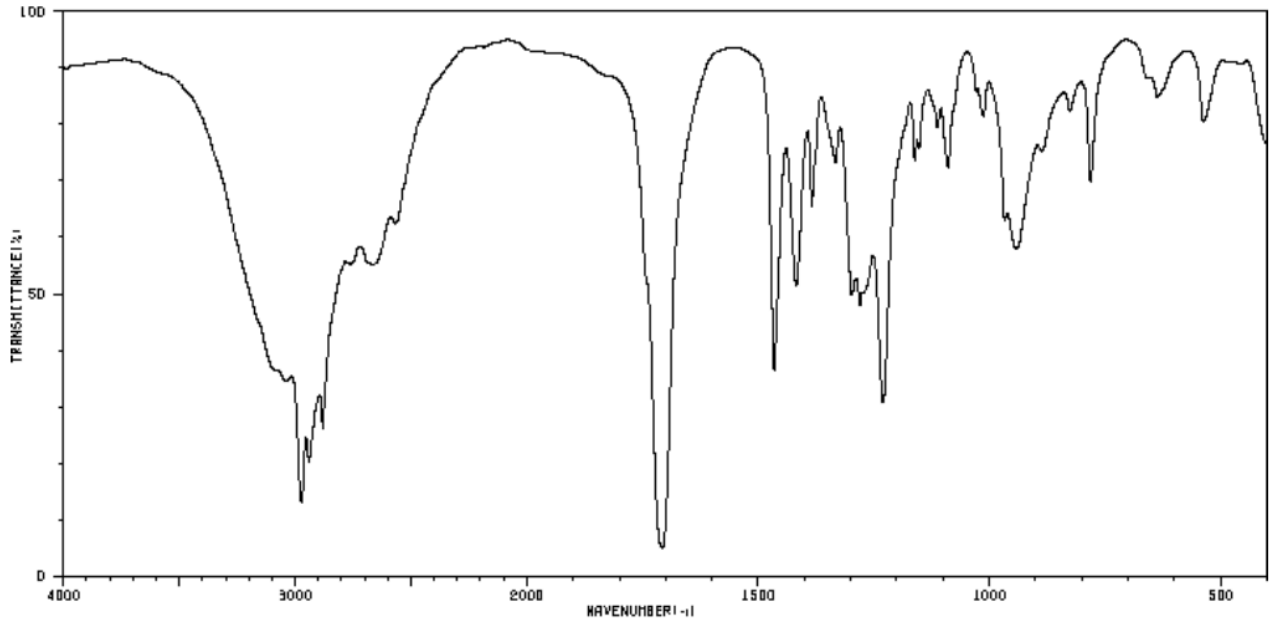
4. $C_8H_{11}N$



5. C_7H_7Cl

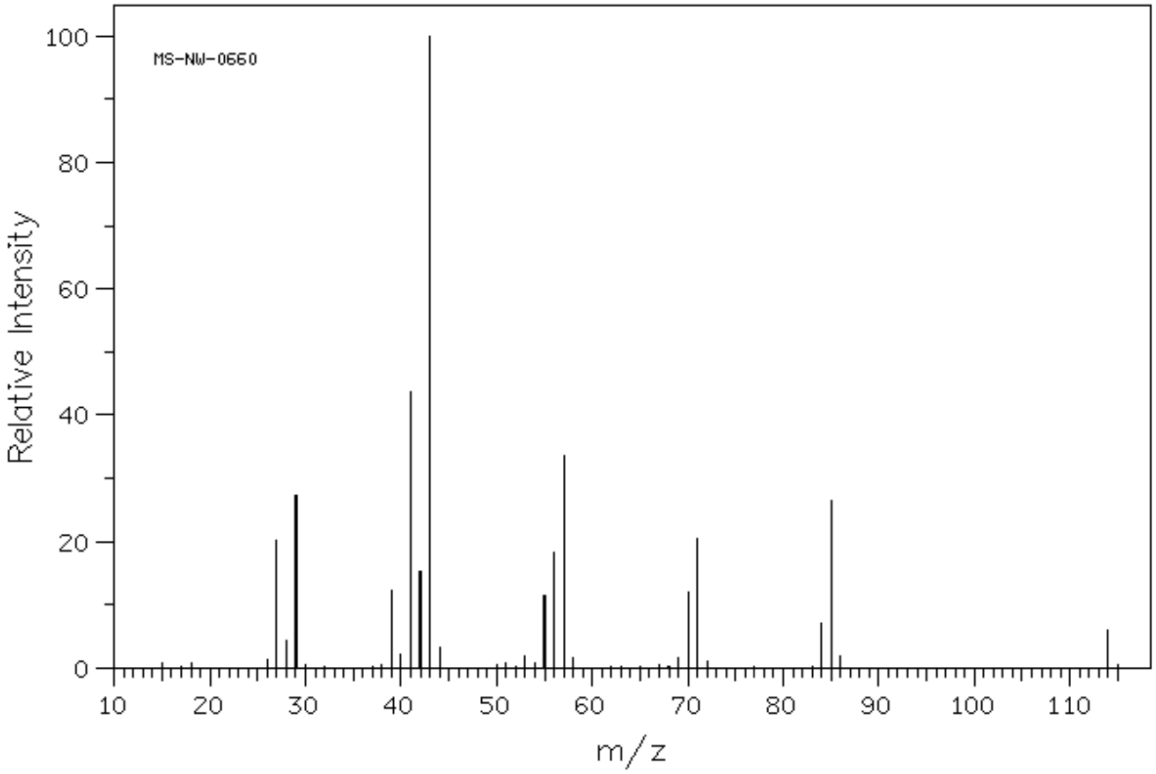


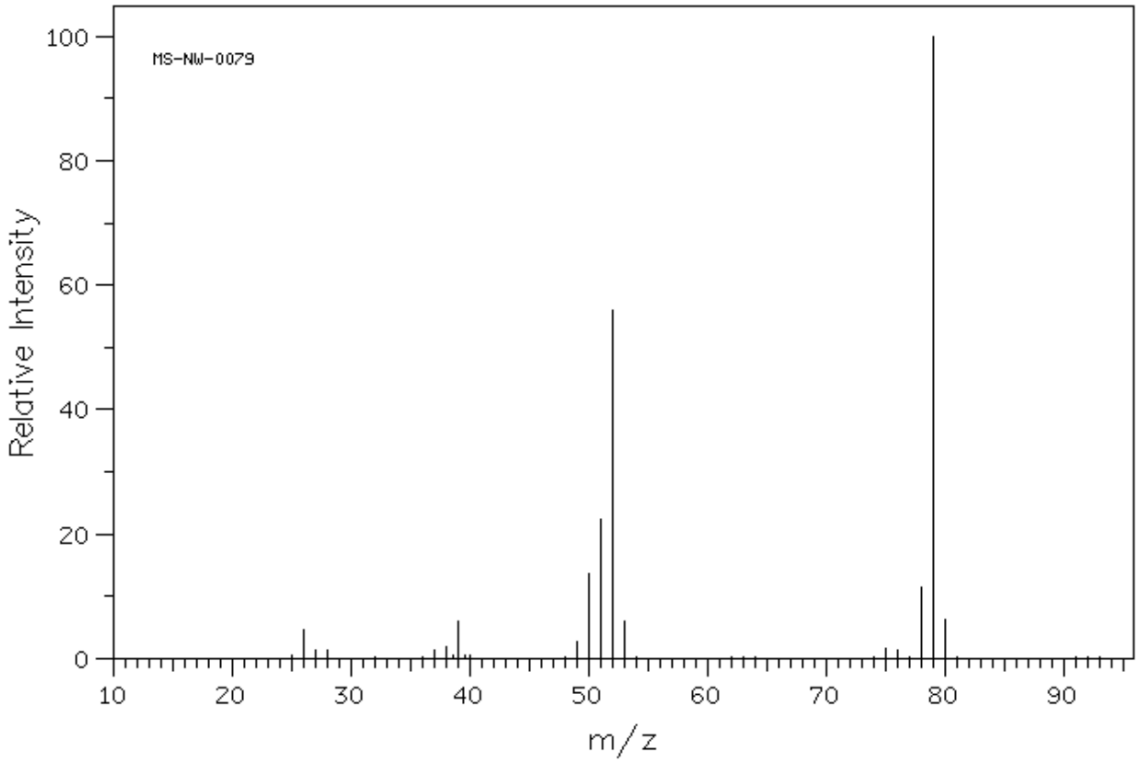
6. $C_5H_{10}O_2$

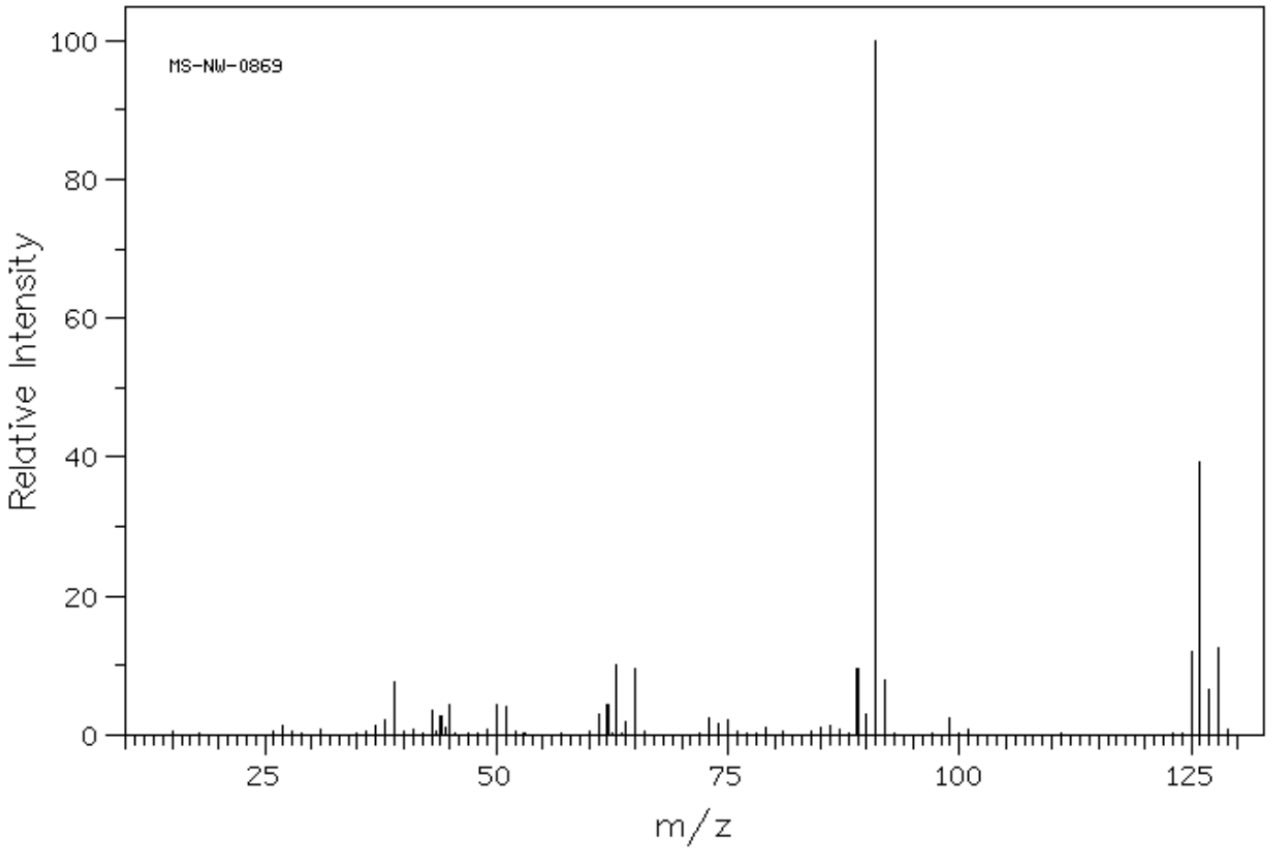


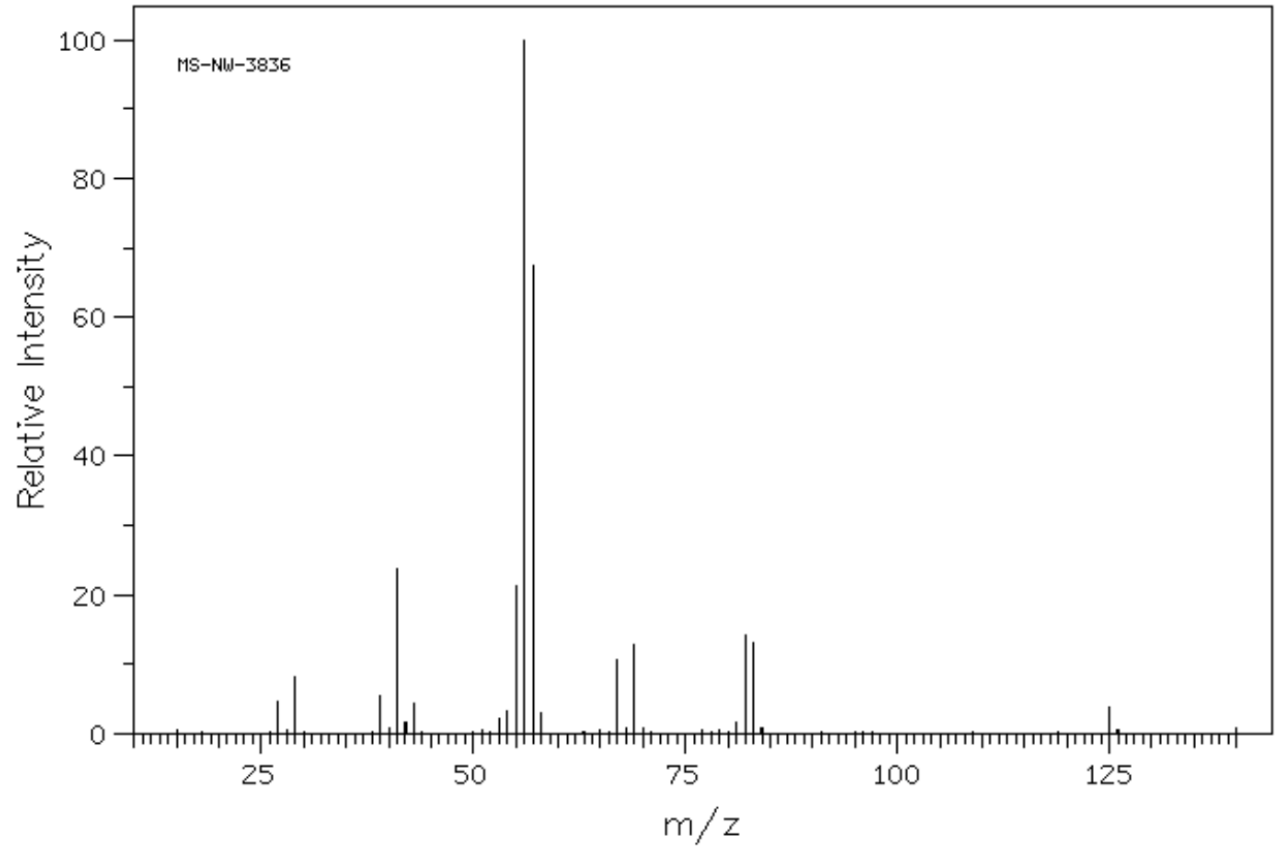
20: ANALYZING M+ AND M+2 PEAKS

For each of the mass spectra, identify the molecular weight of the molecule and determine if it contains N, Cl, or Br.









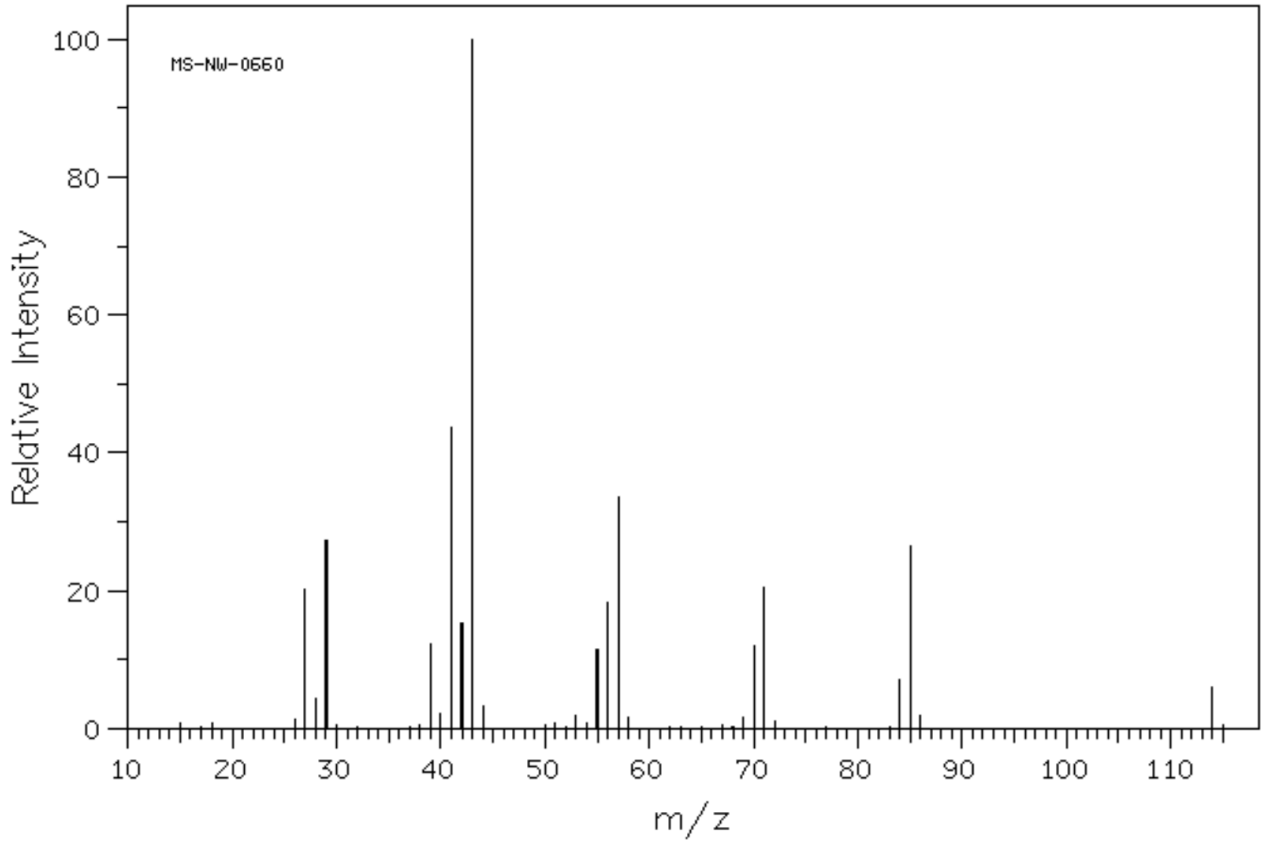
21: HYDROGEN DEFICIENCY INDEX (HDI)

1. Calculate the HDI for C_4H_8. Propose two structures consistent with this formula.

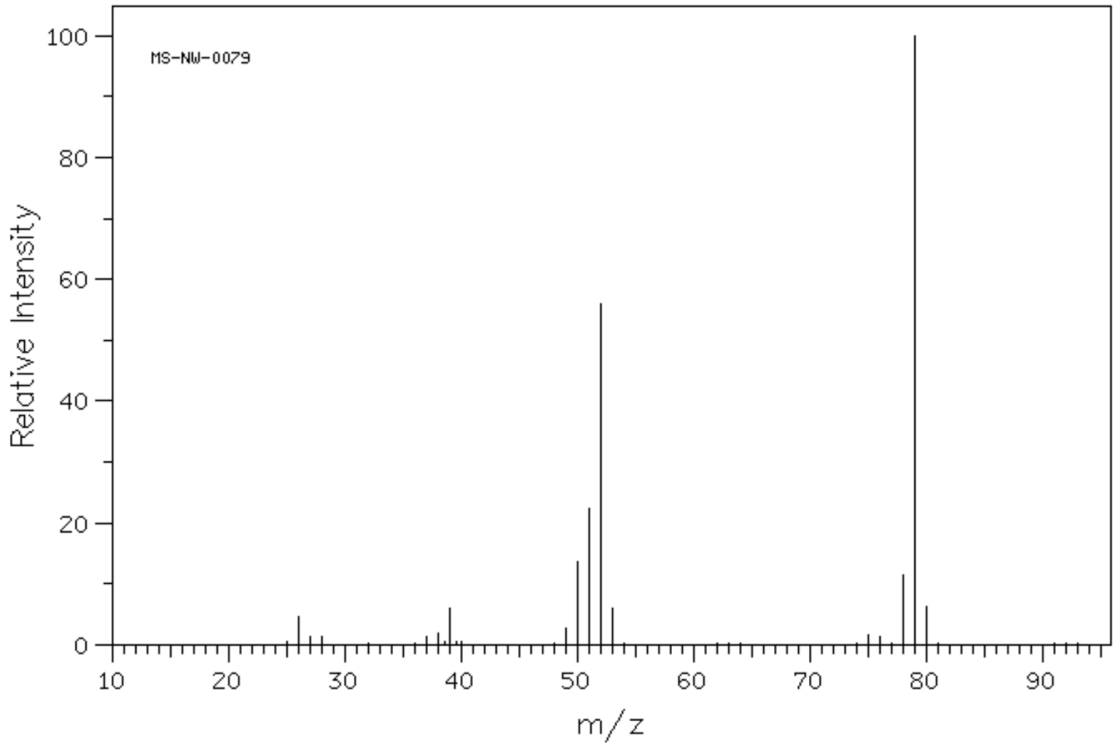
2. Calculate the HDI for $C_6H_{10}O_2$. Propose two structures consistent with this formula.

3. Calculate the HDI for C_7H_8NCl. Propose two structures consistent with this formula.

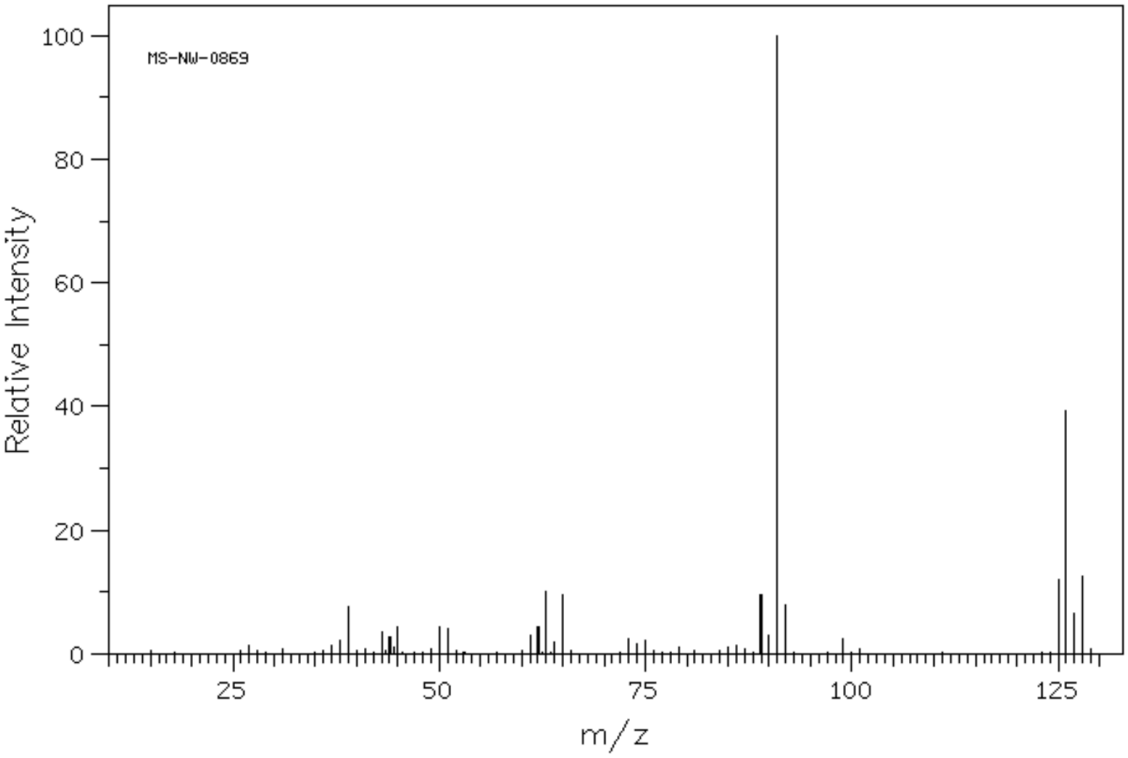
4. For the following mass spec, use the Rule of 13 to determine the molecular formula. Calculate the HDI and propose a structure that is consistent with the mass spec.



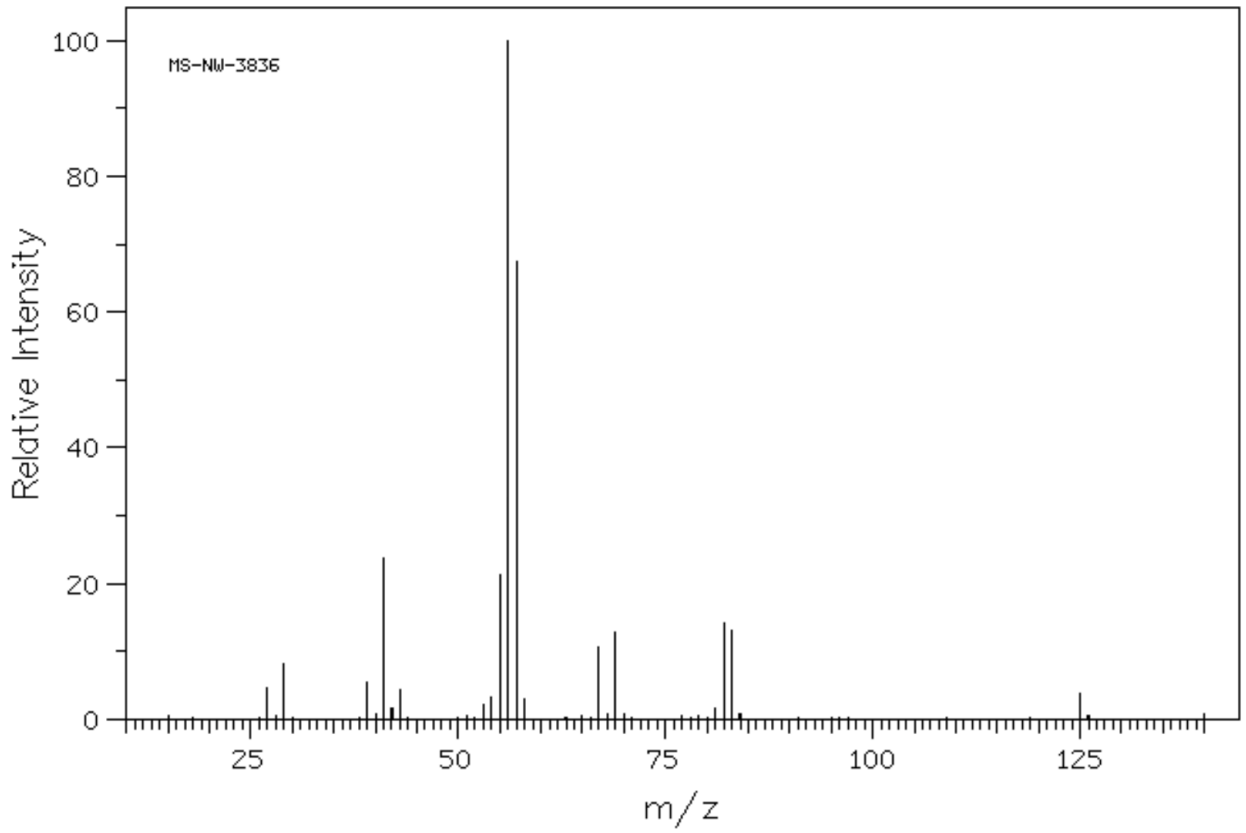
5. For the following mass spec, use the Rule of 13 to determine the molecular formula. Calculate the HDI and propose a structure that is consistent with the mass spec.



6. For the following mass spec, use the Rule of 13 to determine the molecular formula. Calculate the HDI and propose a structure that is consistent with the mass spec.

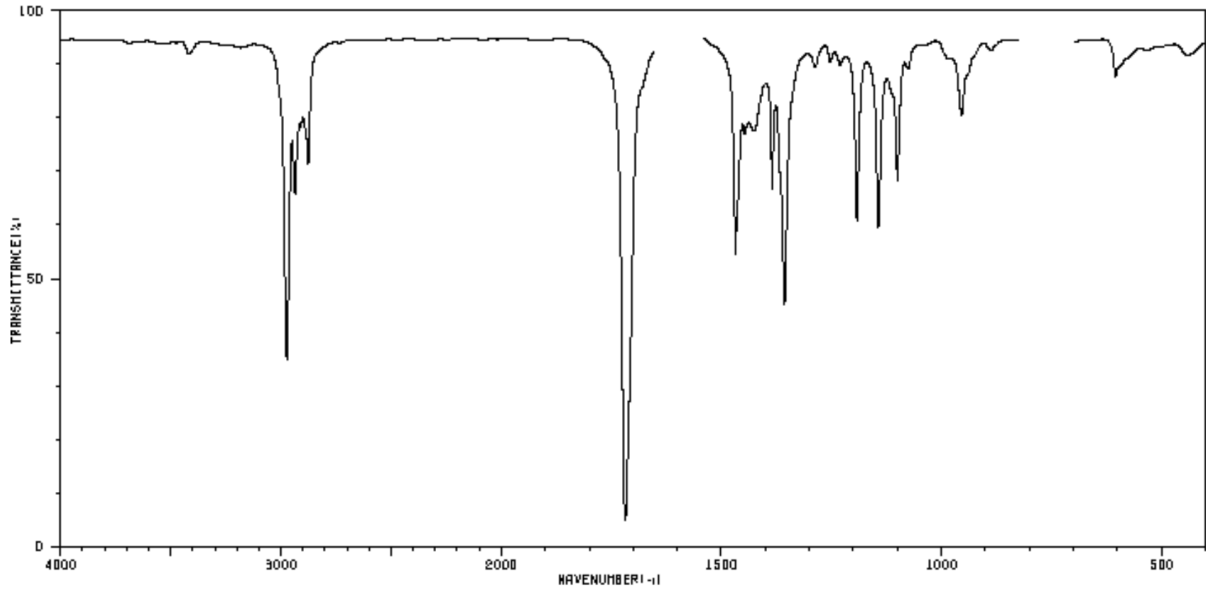


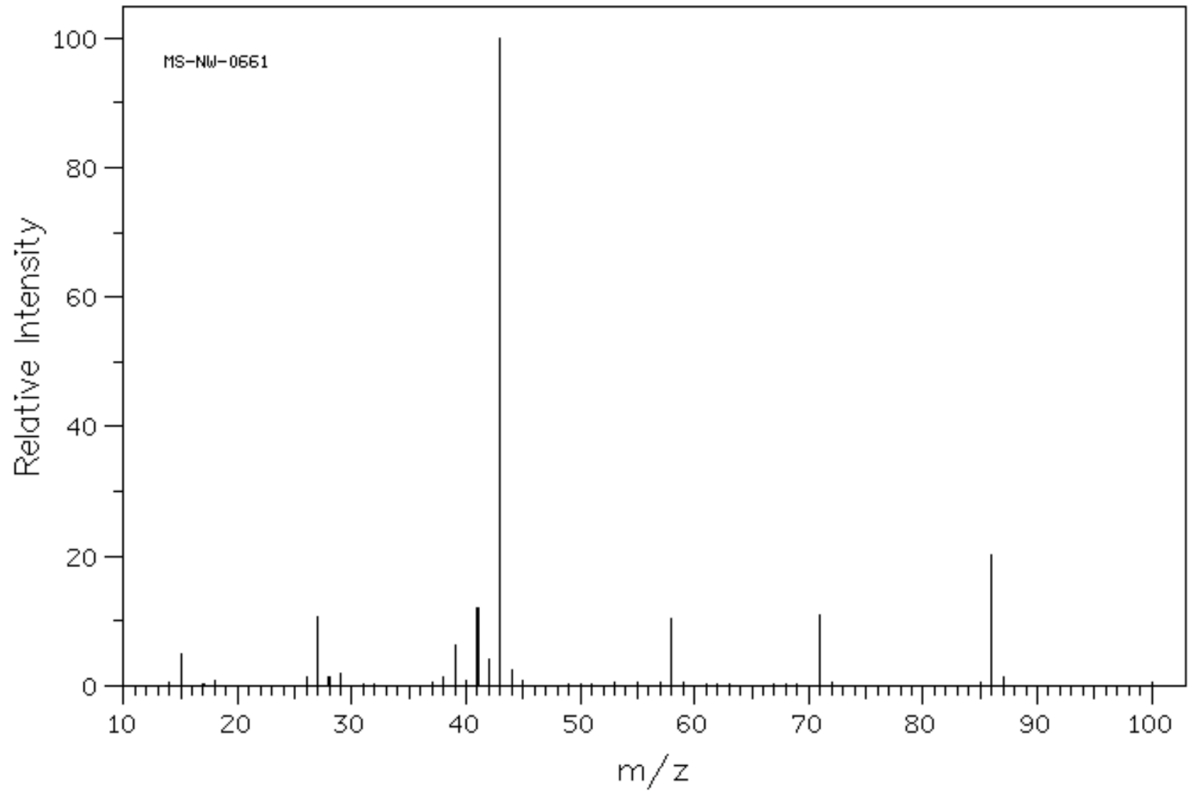
7. For the following mass spec, use the Rule of 13 to determine the molecular formula. Calculate the HDI and propose a structure that is consistent with the mass spec.

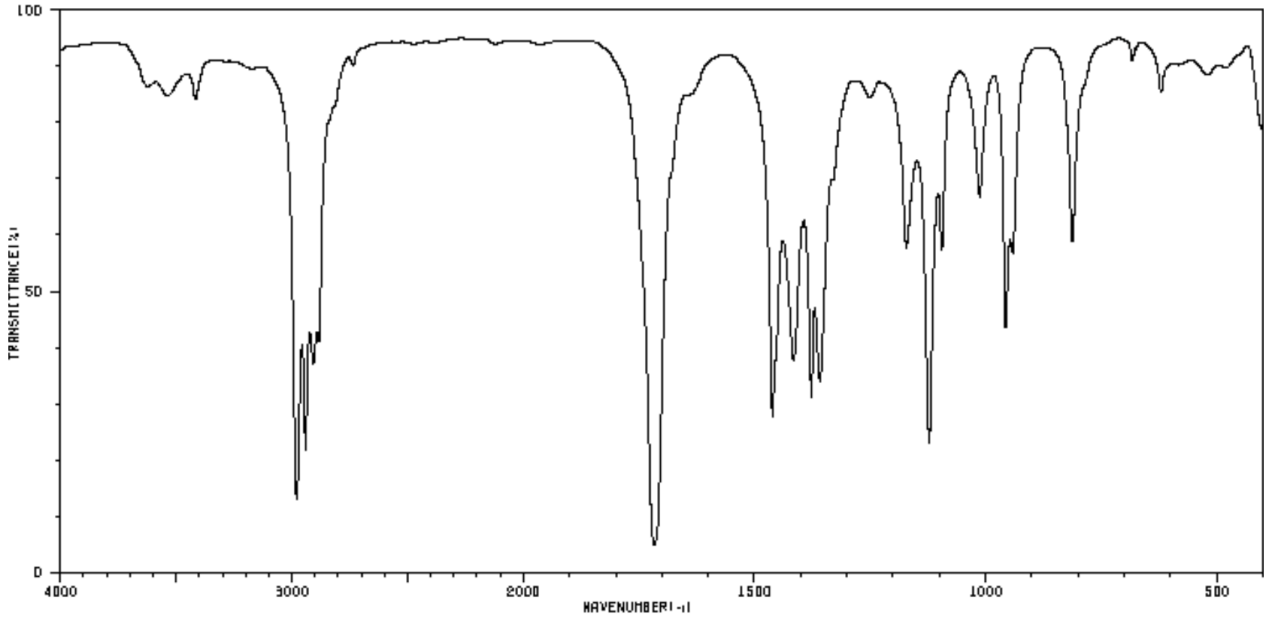


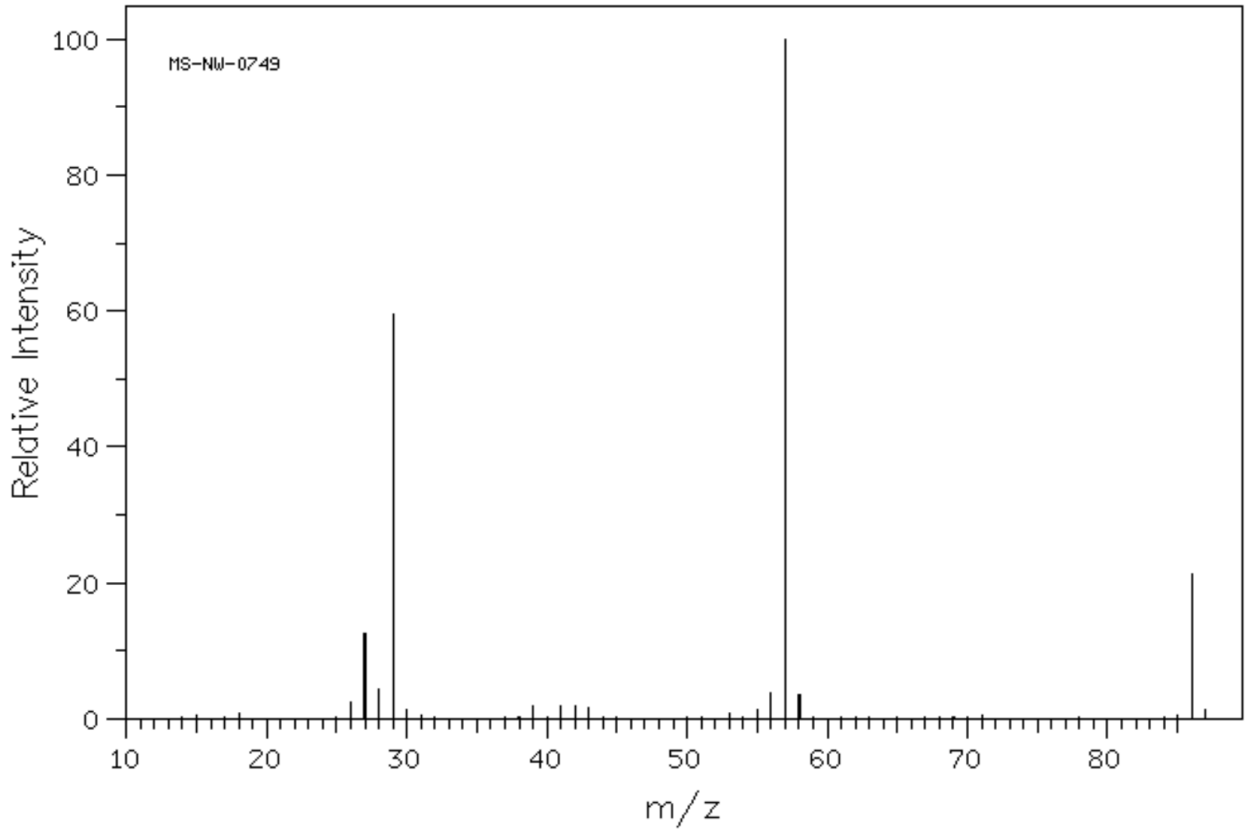
22: COMBINED SPECTRA: IR AND MS

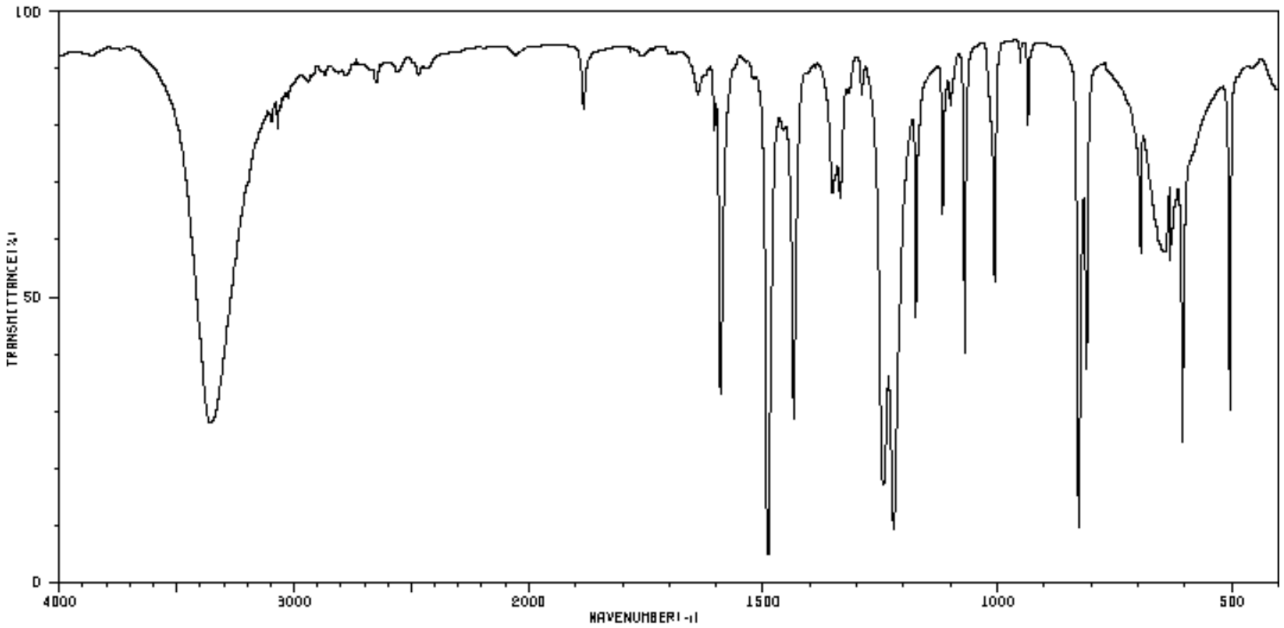
Each page contains the IR and MS for a molecule. Use the spectra together to propose a reasonable structure for the molecule.

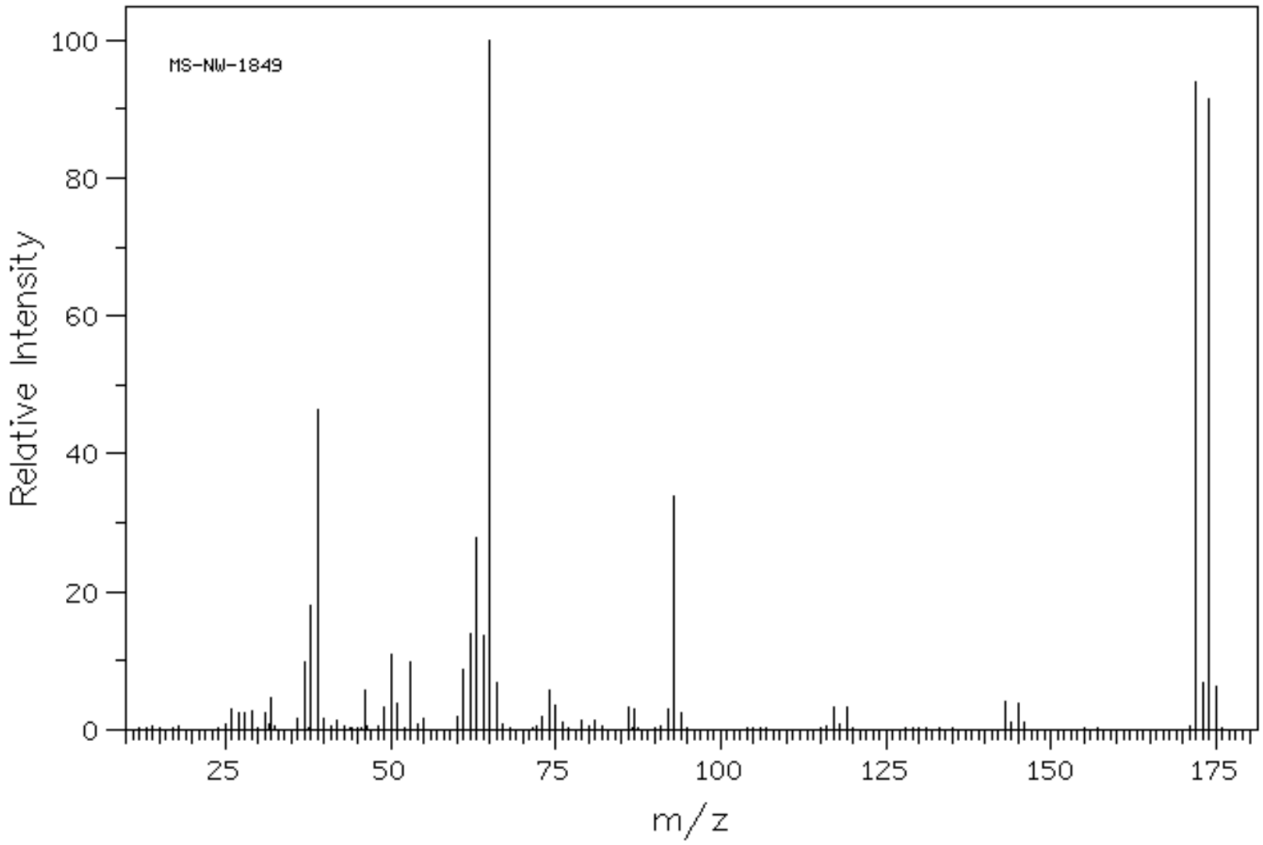


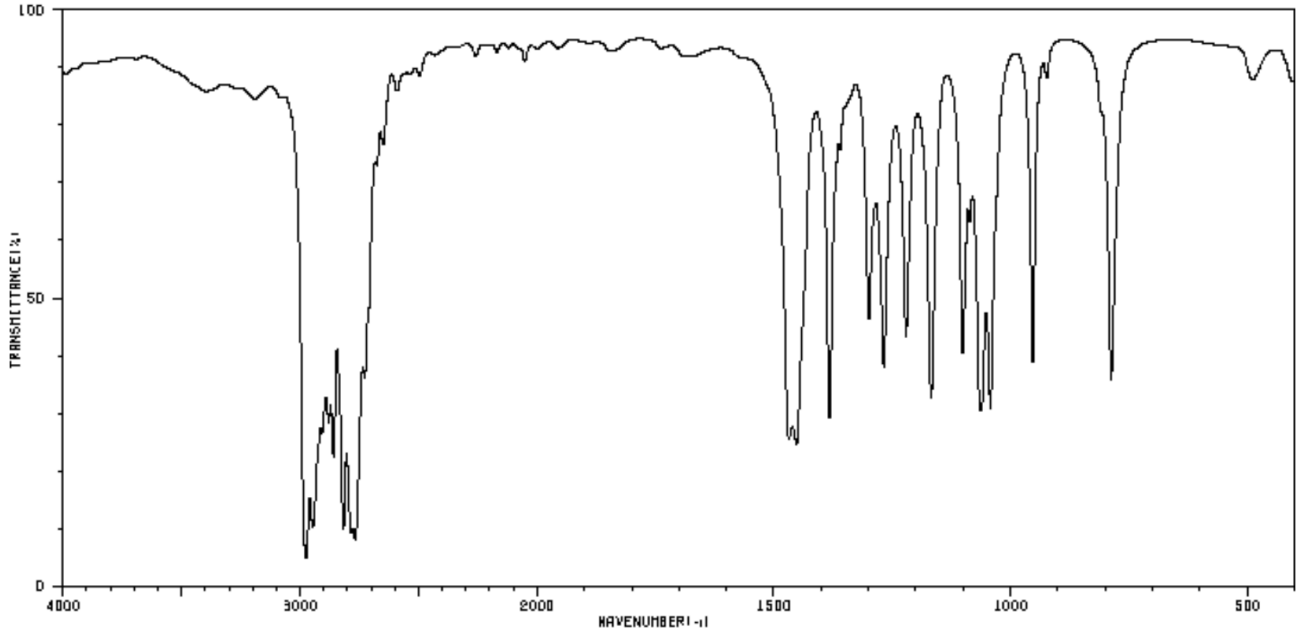


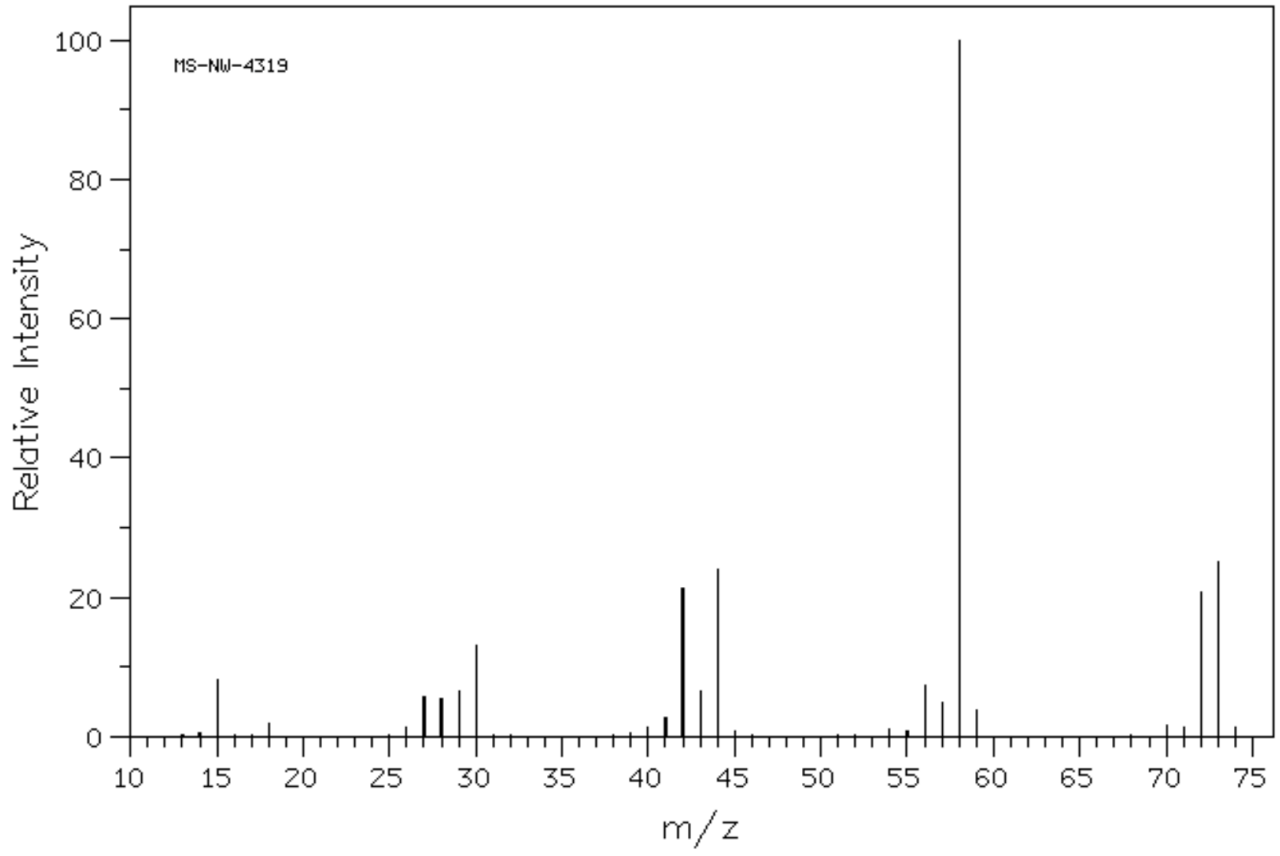












15: NUCLEAR MAGNETIC RESONANCE SPECTROSCOPY (NMR)

MAIN IDEA

Organic molecules can also be evaluated using nuclear magnetic resonance spectroscopy (NMR). This type of spectroscopy uses radio frequency to determine the number of types of "chemically equivalent" hydrogen atoms or carbon atoms in a molecule. It provides information about whether or not a molecule contains a benzene ring, a carbonyl group, or an alcohol.

OBJECTIVES

- Understand the concept of chemical equivalency
- Learn how to interpret the peaks in a proton and carbon NMR spectrum
- Understand integration as it applies to proton NMR spectroscopy, and learn how to use integrals to obtain information about a molecular structure
- Understand the concept of splitting in NMR spectroscopy, and learn how to use the n+1 Rule as a shortcut to predict or interpret splitting
- Learn how to combine data from IR, MS, and NMR spectra to propose molecular structures

SKILLS TO MASTER

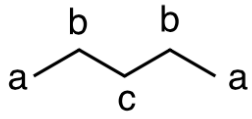
- Identify equivalent protons and equivalent carbons in a molecule
- Identify the general location of NMR peaks associated with carbons and hydrogens in alkanes, alcohols, aldehydes, ketones, and benzene rings
- Use the integrals of a proton NMR spectrum to determine the ratio of chemically-equivalent protons in a molecule
- Use the n+1 to predict and interpret splitting in a proton NMR spectrum
- Use combined spectral data to propose molecular formulas and molecular structures

TERMINOLOGY

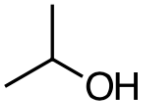
- Chemical shift
- Chemically equivalent
- Coupling
- Complex splitting
- Deshielding
- n+1 Rule
- Shielding
- Splitting

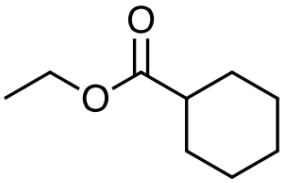
23: PREDICTING THE NUMBER OF PEAKS (SIGNALS) IN A ^{1}H-NMR SPECTRUM

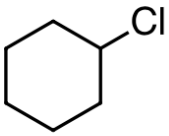
For each of the following molecules, predict the number of signals that would be present in the ^{1}H-NMR (proton NMR) spectrum. Label the equivalent protons as shown in the example.

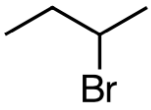


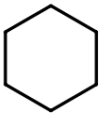
3 signals











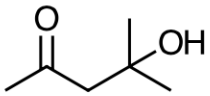
24: CHEMICAL SHIFT AND INTEGRATION

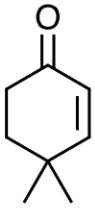
1. For each molecular structure below, identify the types of equivalent protons and label them a, b, c, etc.

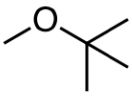
2. Match each structure (on the following pages) to the correct ^{1}H-NMR spectrum. To do this, use the number of peaks in the spectrum and the number of types of equivalent protons in each structure.

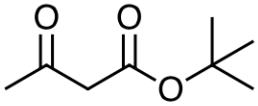
3. For each spectrum, match each peak to the correct group of equivalent protons. Label the peaks a, b, c, etc. based on the labels you assigned in problem 1.

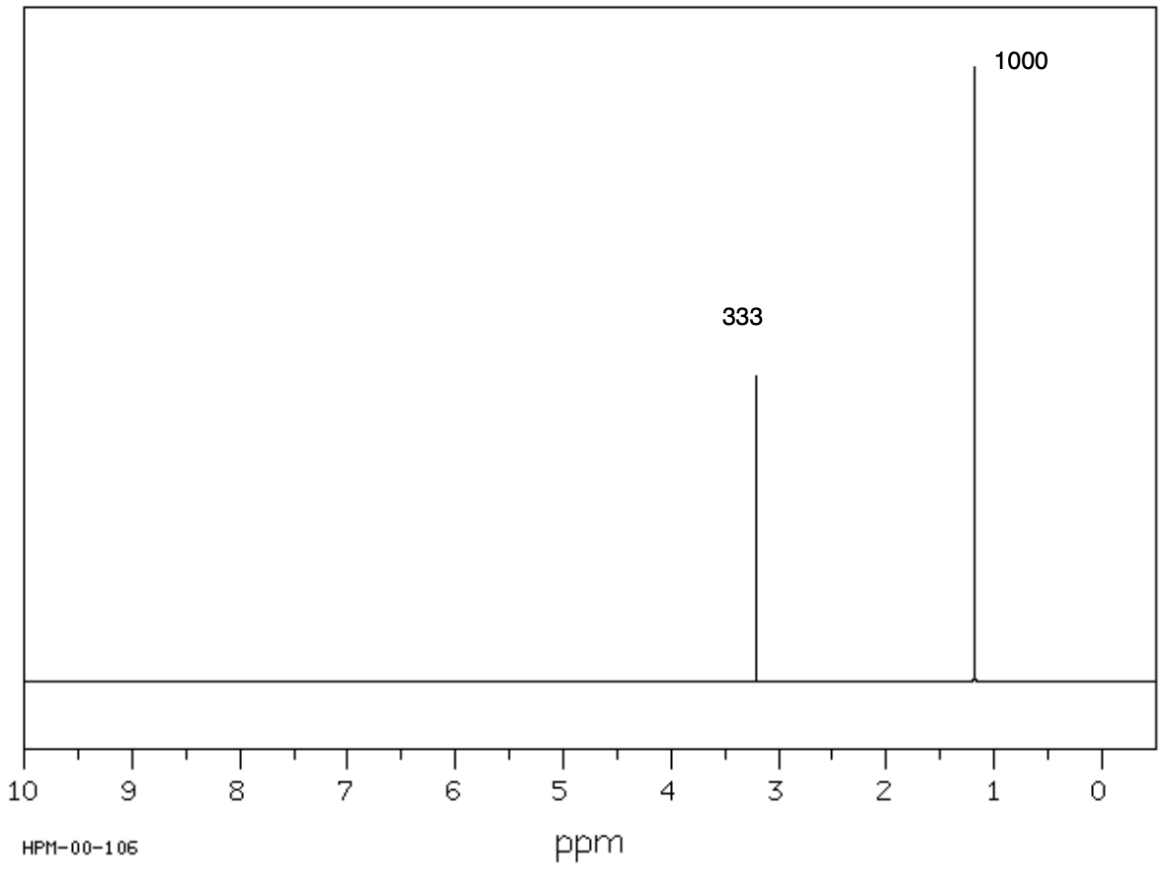
4. Calculate the integration of each peak and make sure it is consistent with the assignments you made in problem 3.

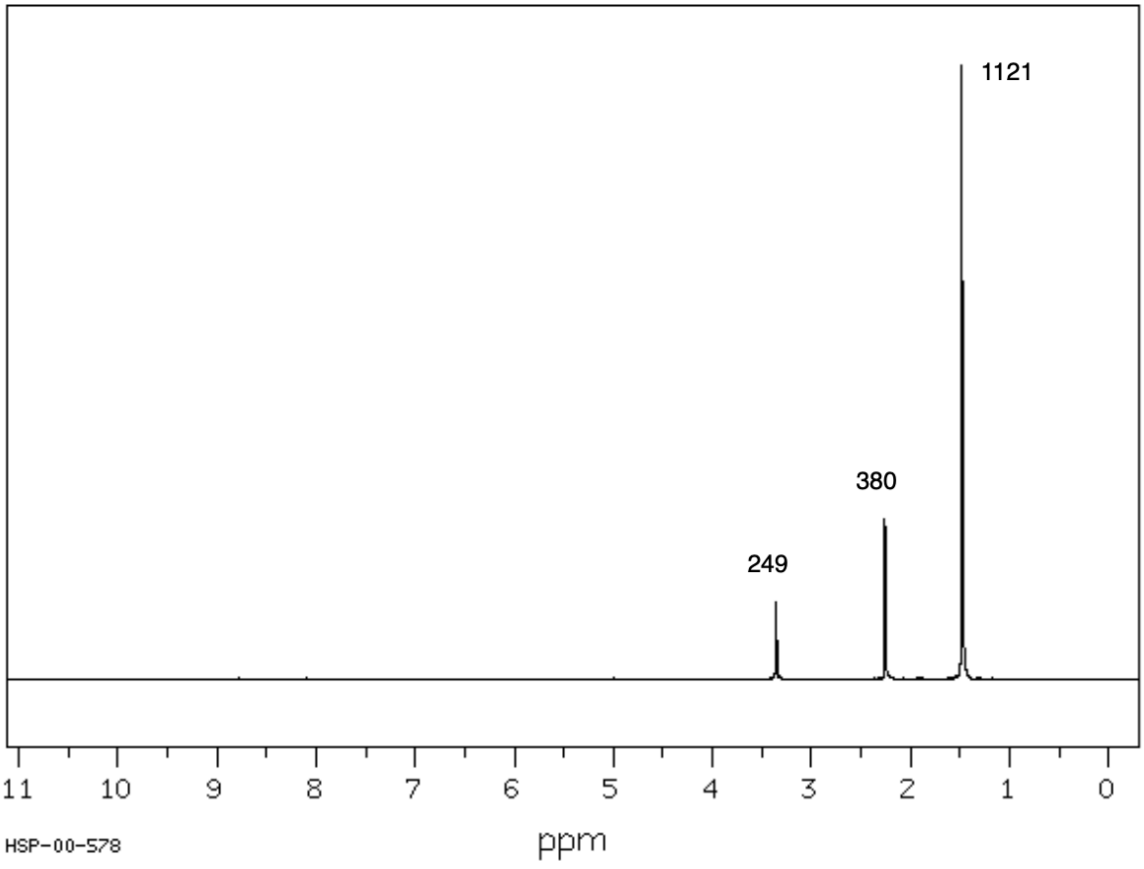


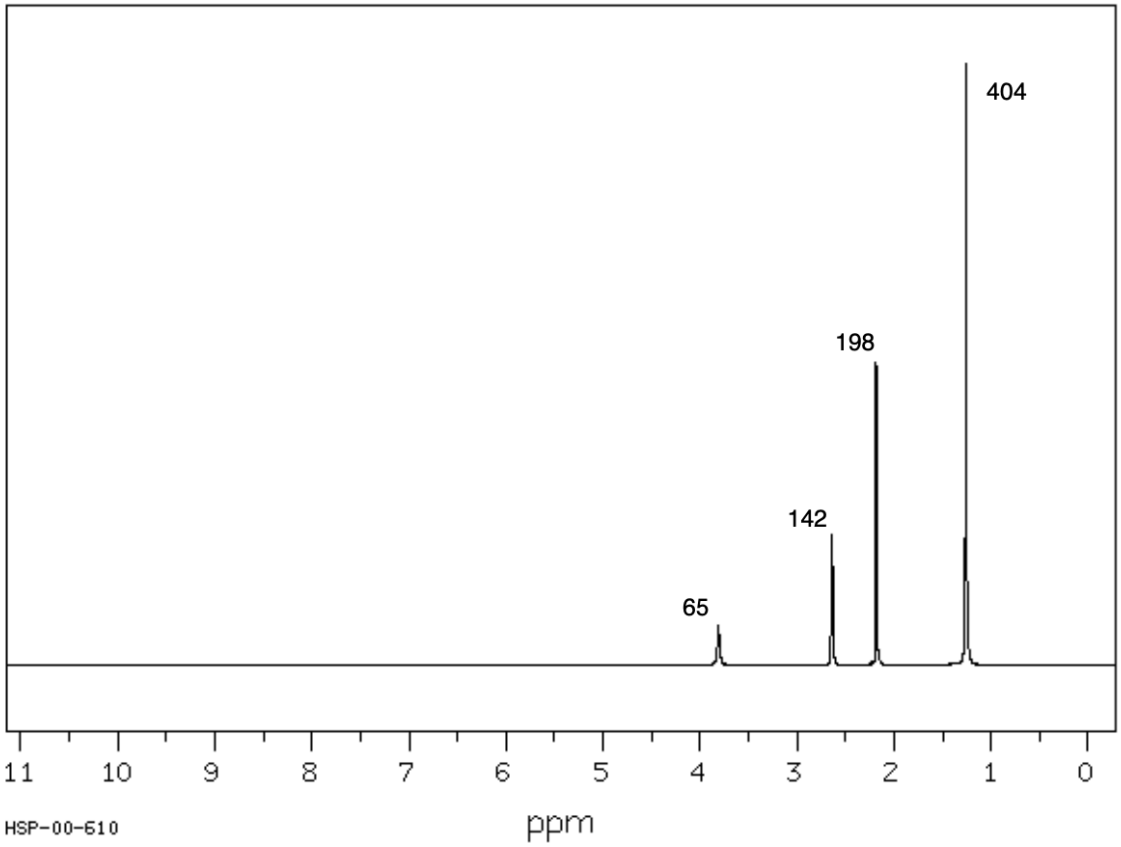


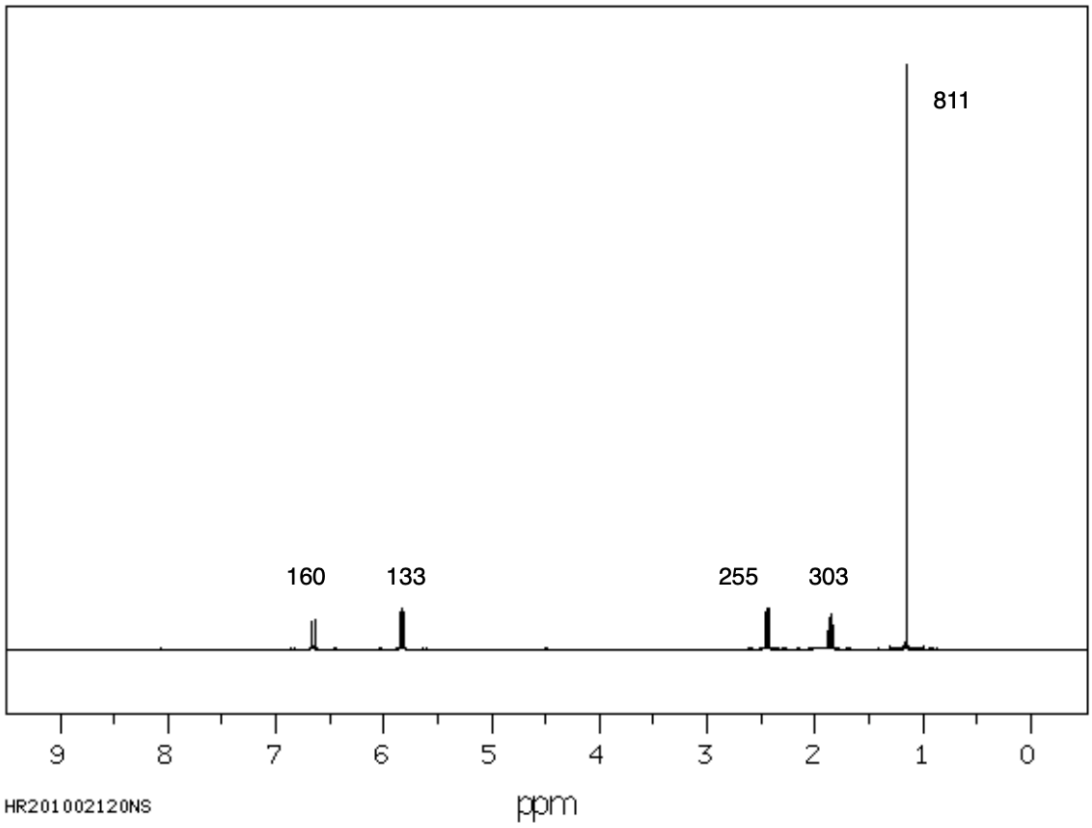






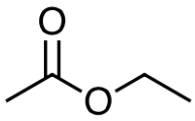


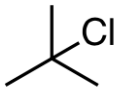


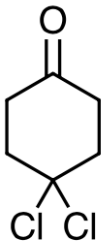


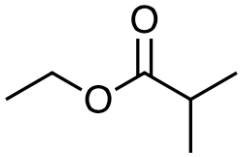
25: SPLITTING AND THE N+1 RULE

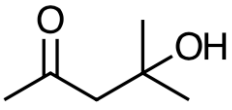
Use the n+1 Rule to predict the splitting for each type of equivalent proton in the following molecules. Alcohol, carboxylic acid, and aldehyde protons are not magnetically coupled to other protons and do not split or cause splitting, even if they are within 3 bonds of another proton.

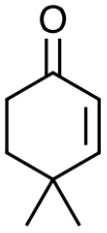


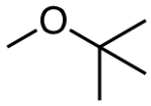








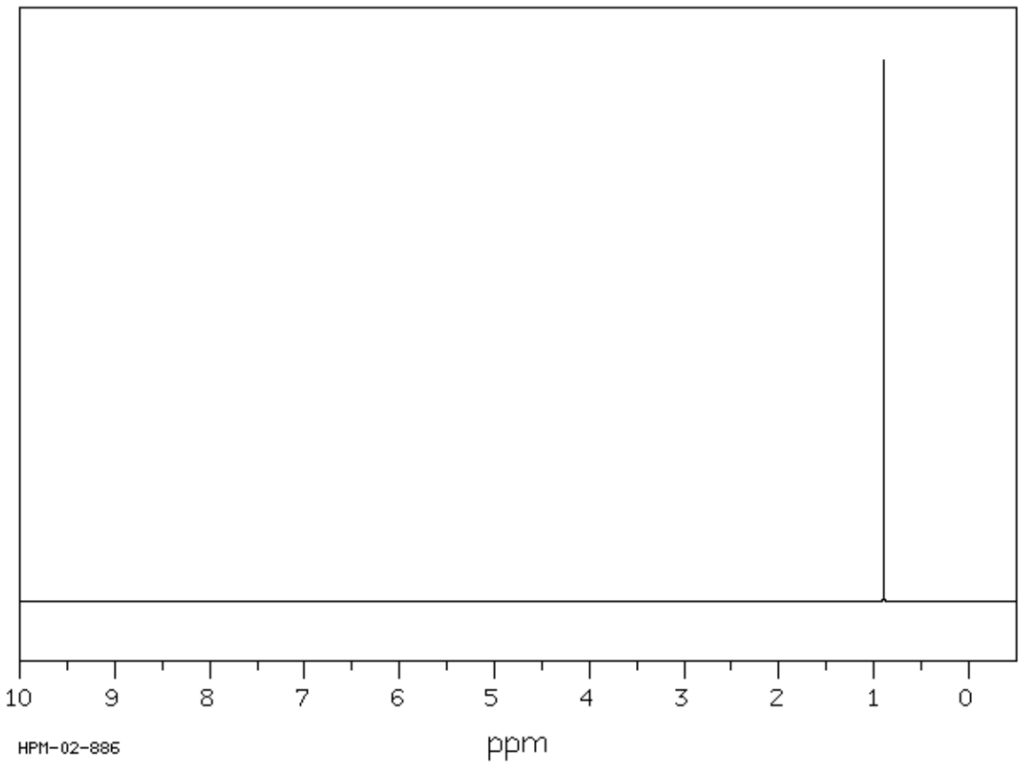




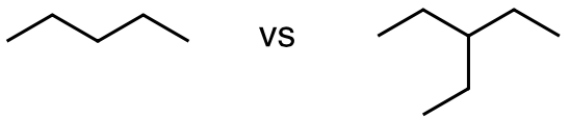
26: USING ^{1}H-NMR TO DISTINGUISH BETWEEN COMPOUNDS

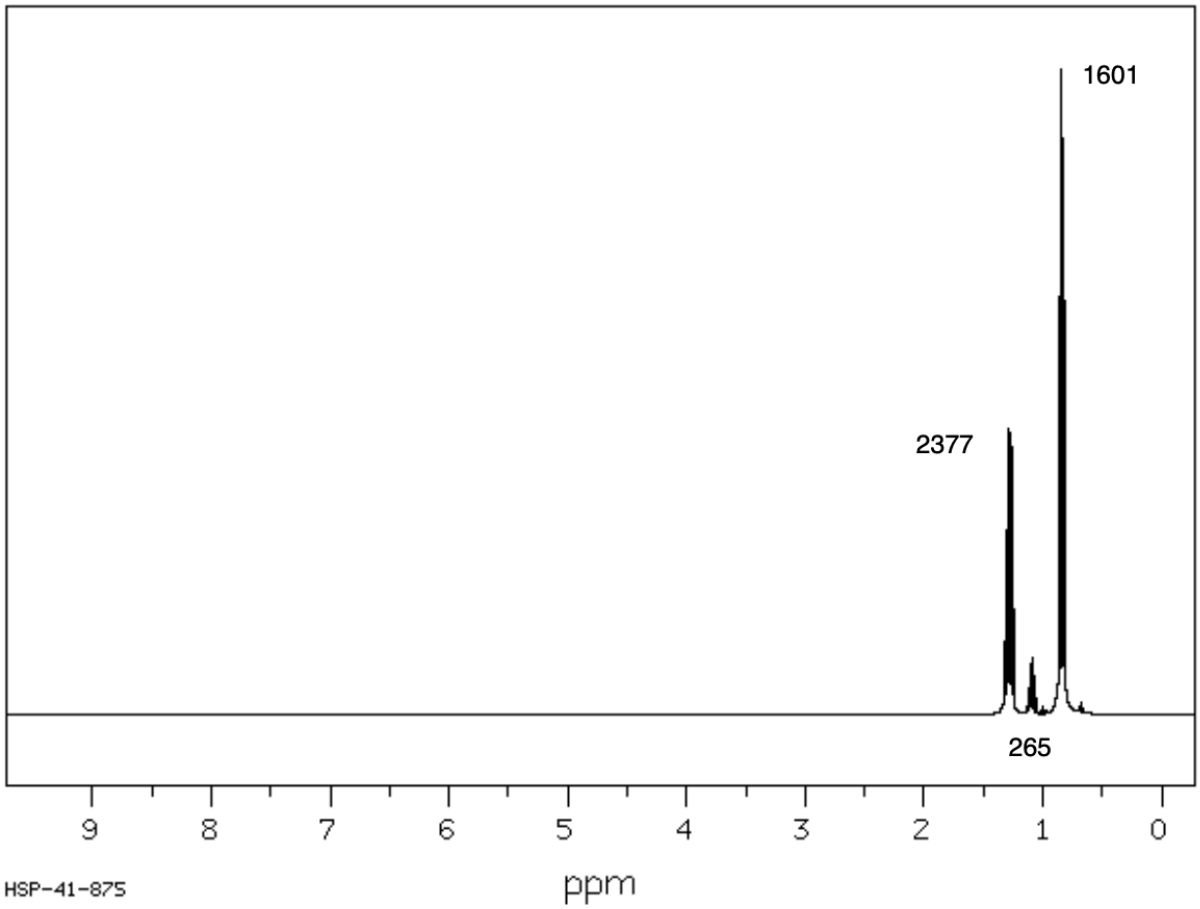
When distinguishing two or more compounds via NMR (for example, matching a structure to a spectrum in a multiple choice question) it isn't always necessary to do a complete analysis. This worksheet will show you two strategies for quickly distinguishing between compounds using NMR.

1. First, attempt to match the number of peaks with the number of types of equivalent hydrogen.



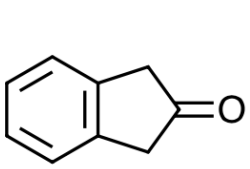
2. If you have more than one compound with the same number of equivalent protons, try using the integration to determine the correct structure.

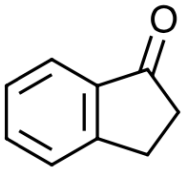


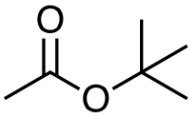


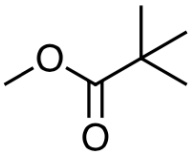
If you are still unable to determine the correct structure, you will need to analyze splitting and/or chemical shift.

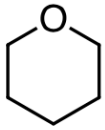
3. For each pair of molecules, identify how you could quickly distinguish them using ^{1}H-NMR spectroscopy.

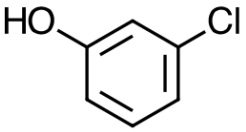


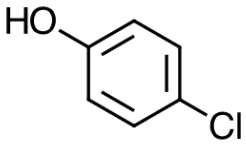








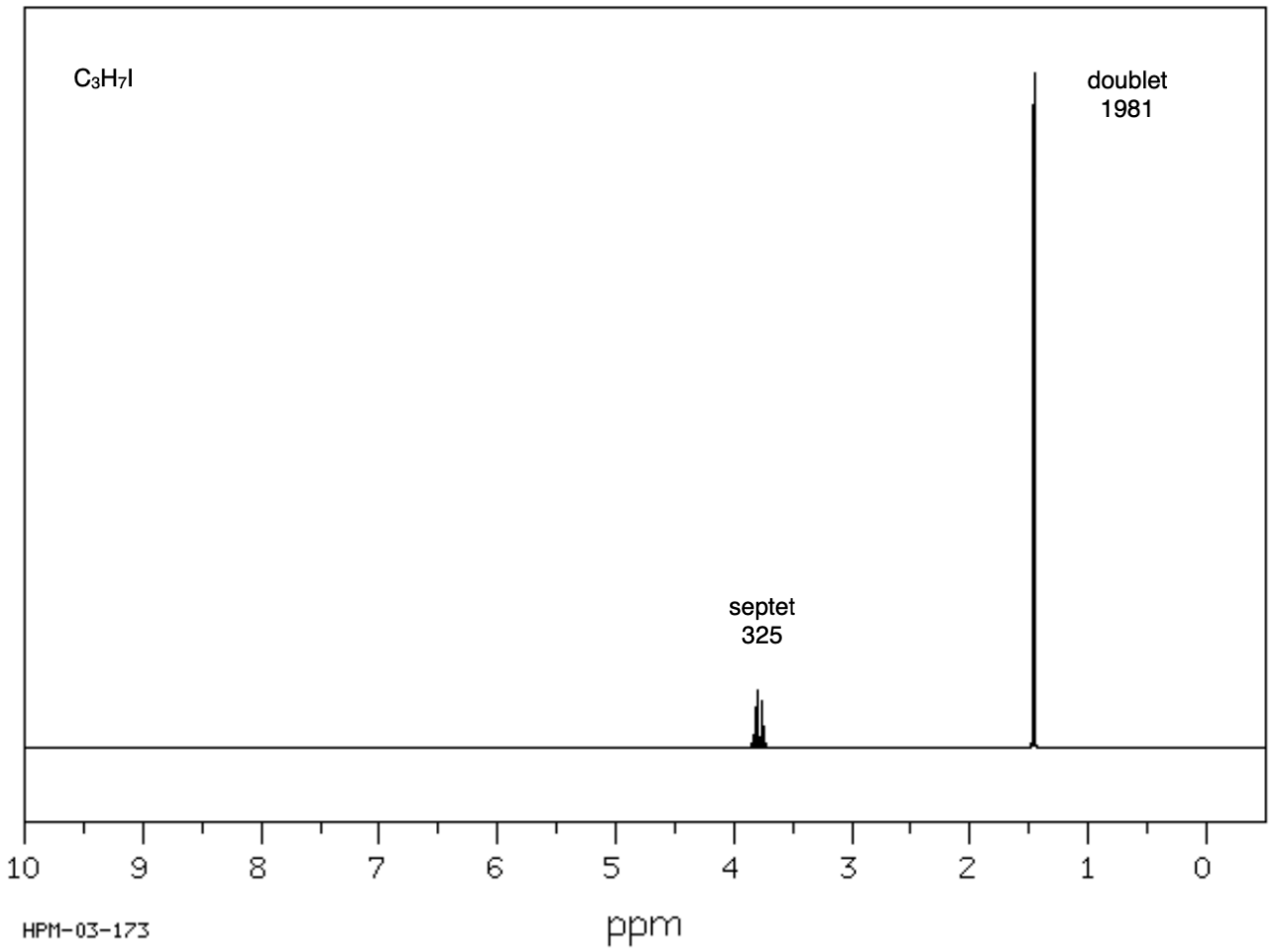


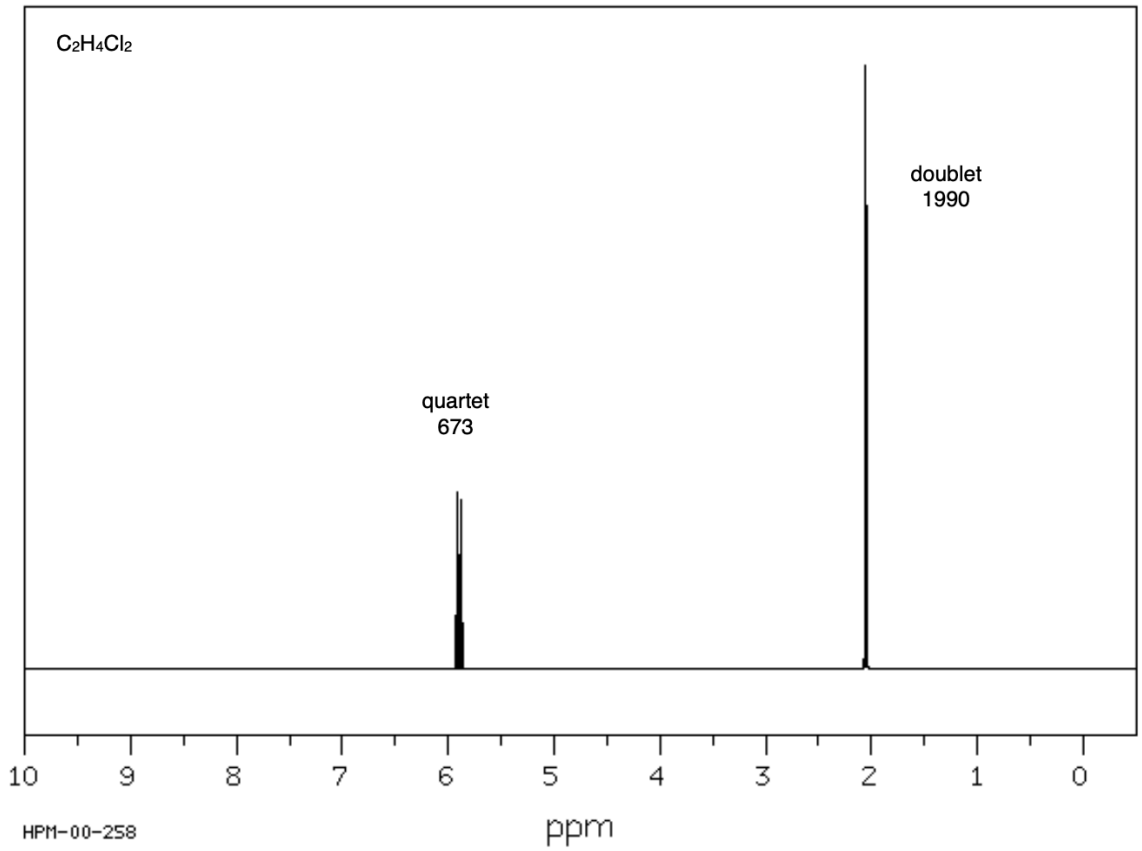


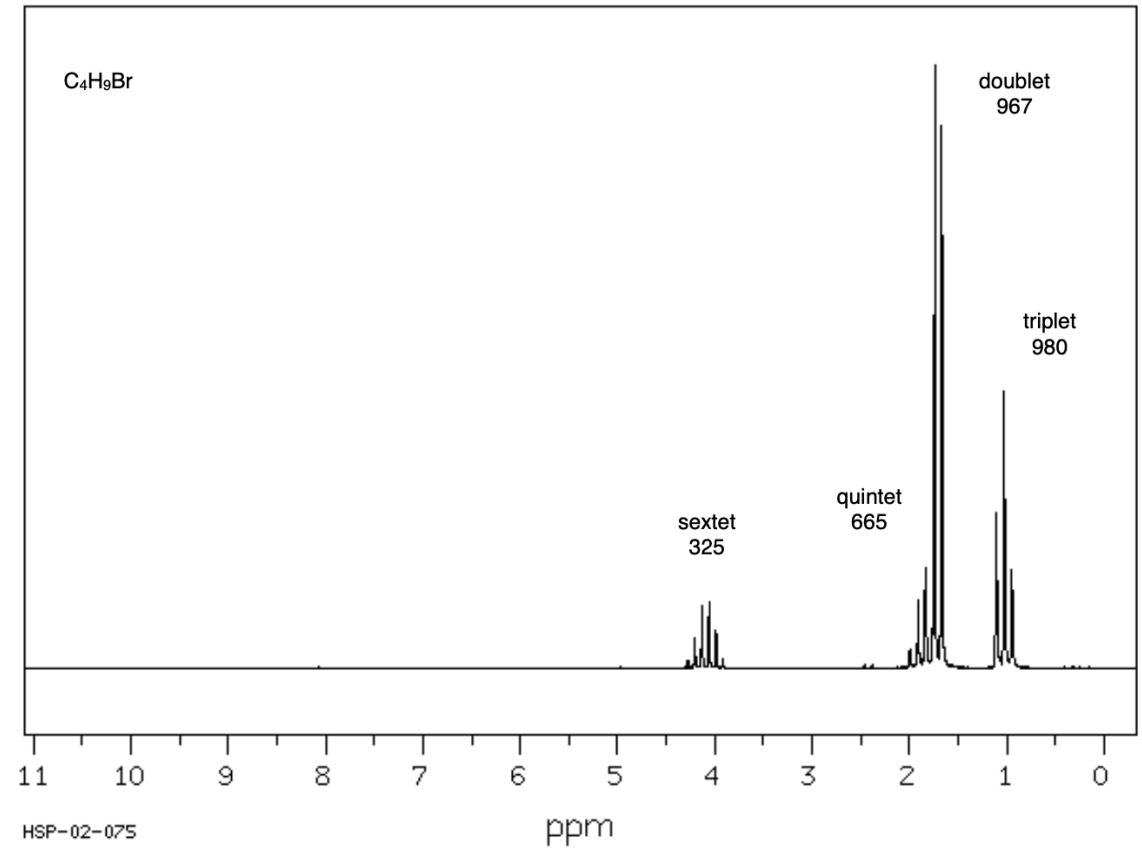
27: BASIC ^{1}H-NMR ANALYSIS

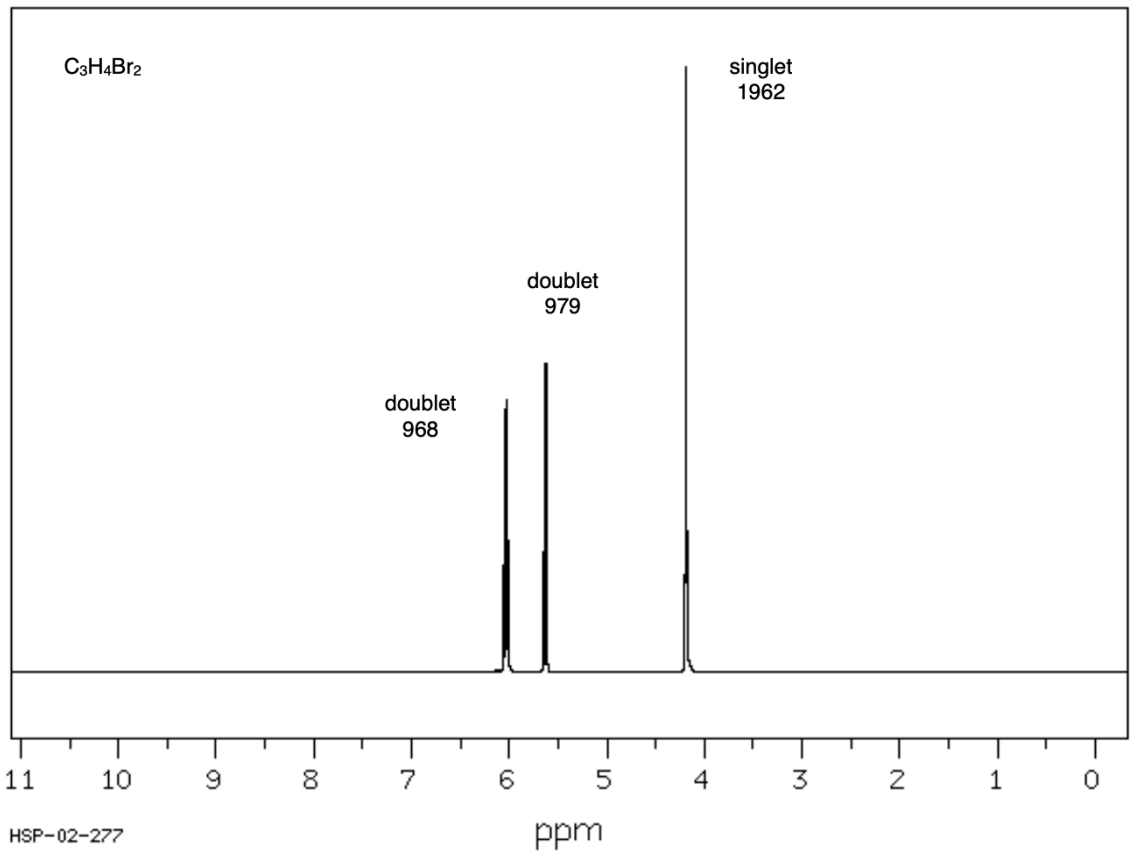
Propose a structure for each of the following spectra. When done correctly, you will only have one possible structure for each spectrum. Follow these steps in your analysis:

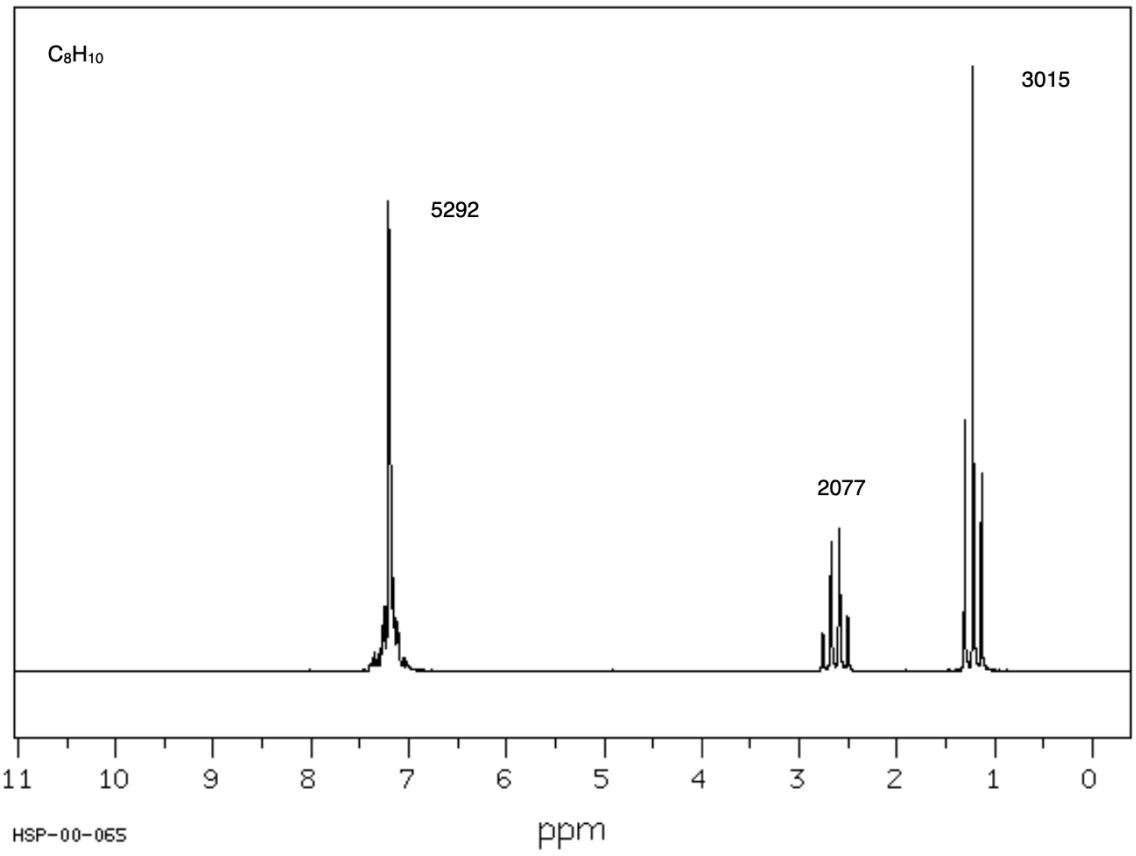
1. Calculate HDI
2. Analyze the integration and compare to the molecular formula to make sure the integration is correct
3. Draw a molecular fragment that accurately represents the splitting and integration of each peak
4. Combine the fragments into the correct structure





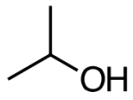


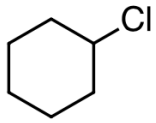


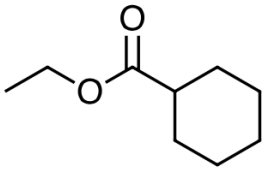


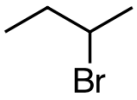
28: PEAKS AND SHIFT IN ^{13}C-NMR

For each of the following molecules, predict the number of signals (peaks) that would be present in the ^{13}C-NMR spectrum. Predict the relative location of each peak. (Which is the furthest left? Which is the furthest right? You do not need to use numerical values.)



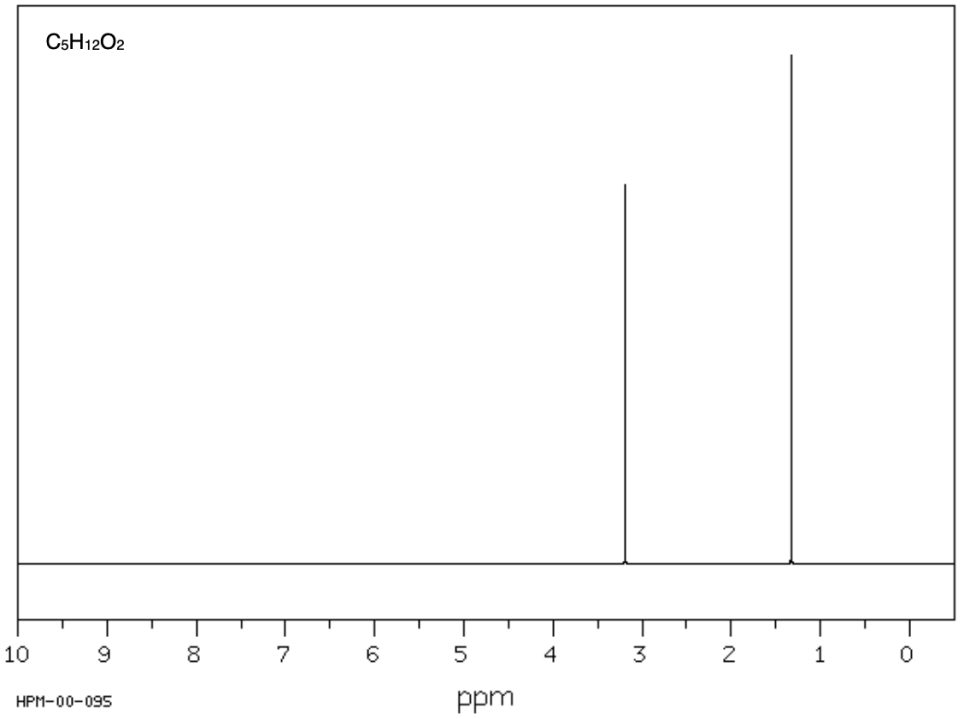


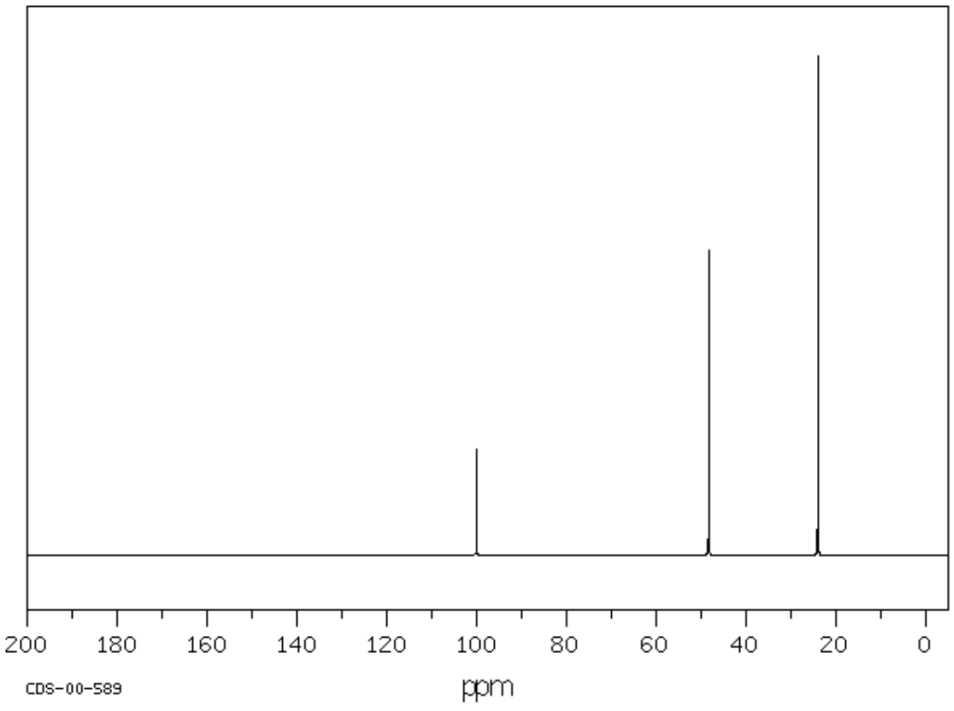


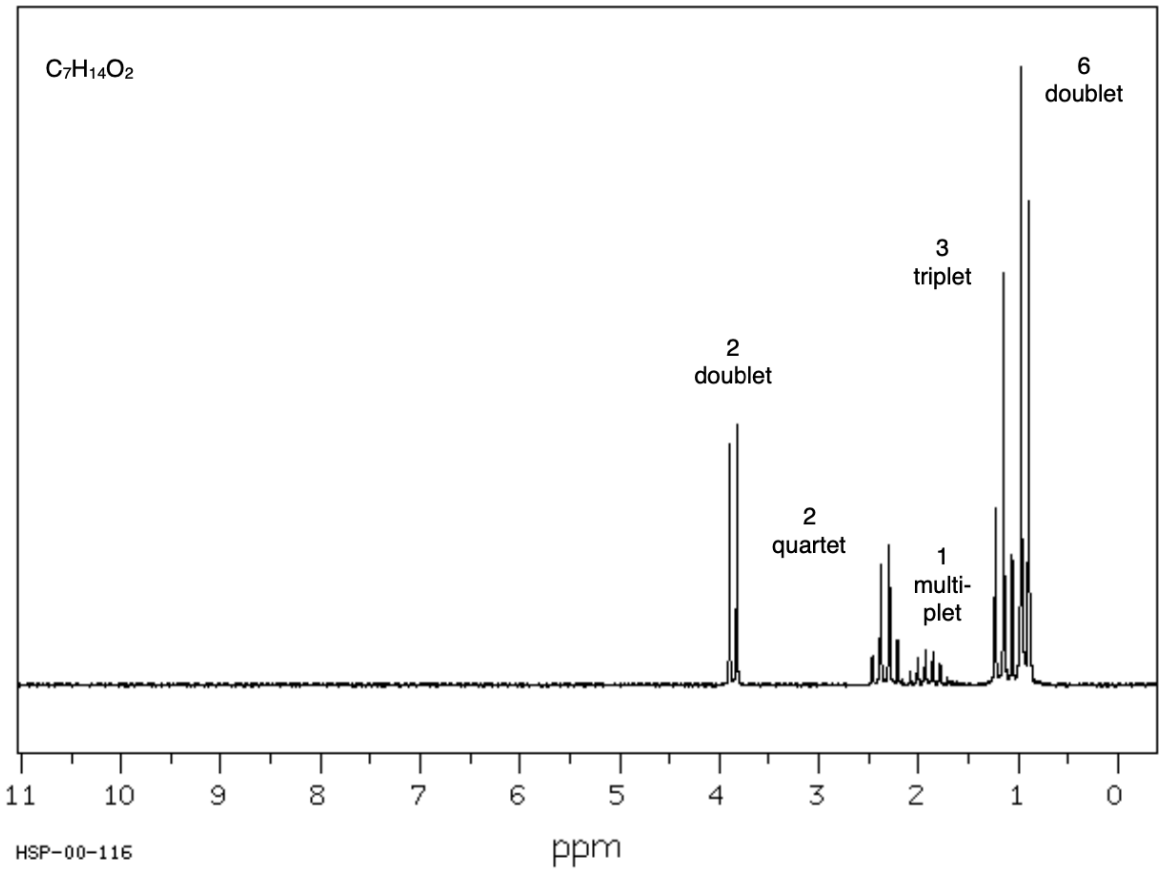


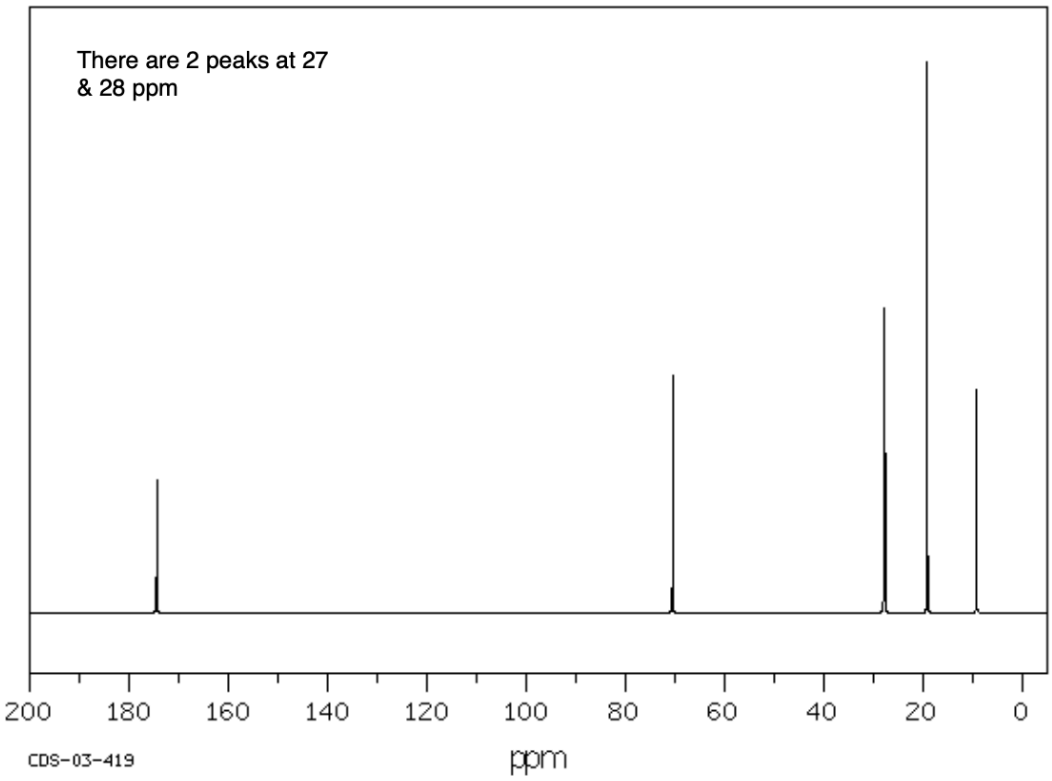
29: COMBINED SPECTRA SETS: ^{1}H-NMR AND ^{13}C-NMR

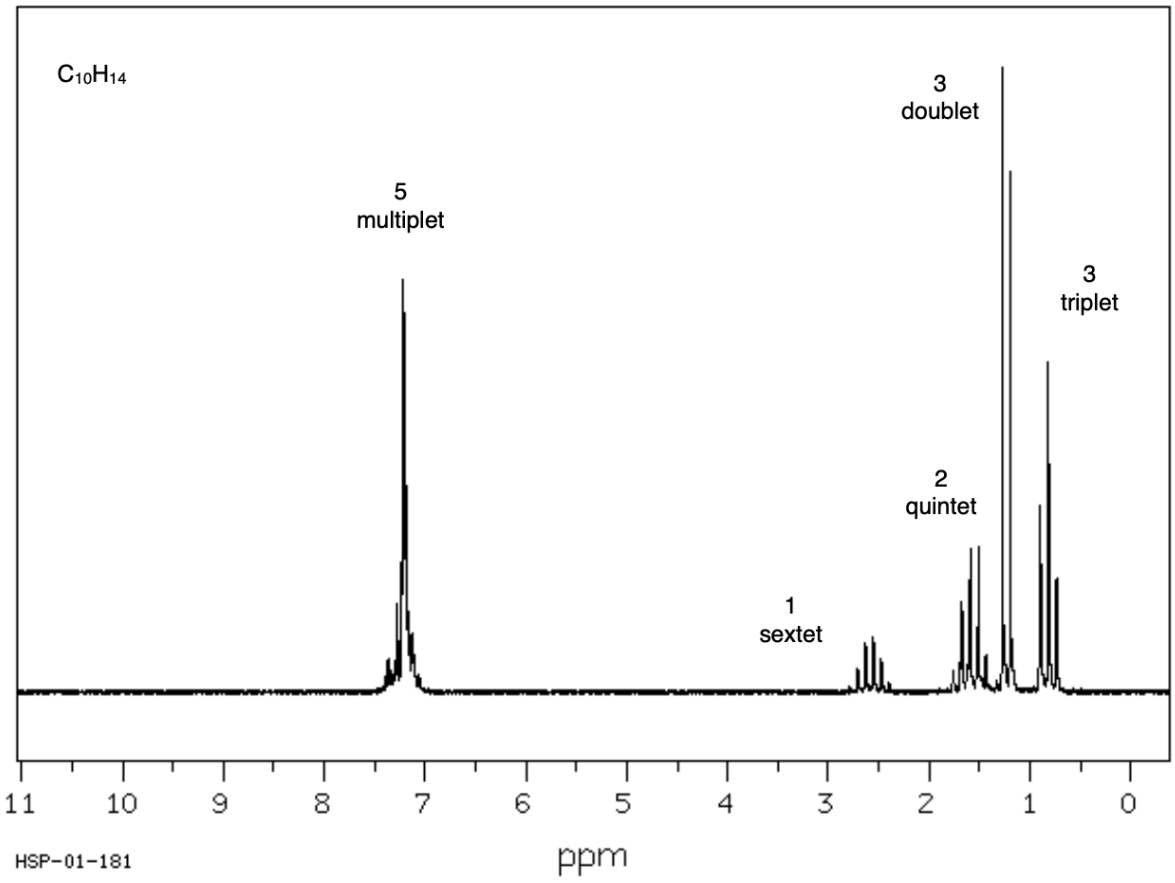
Each page has a ^{1}H-NMR (on top) and a ^{13}C-NMR (on bottom) that correspond to the same molecule. The molecular formula has been provided. Determine the structure of each molecule.

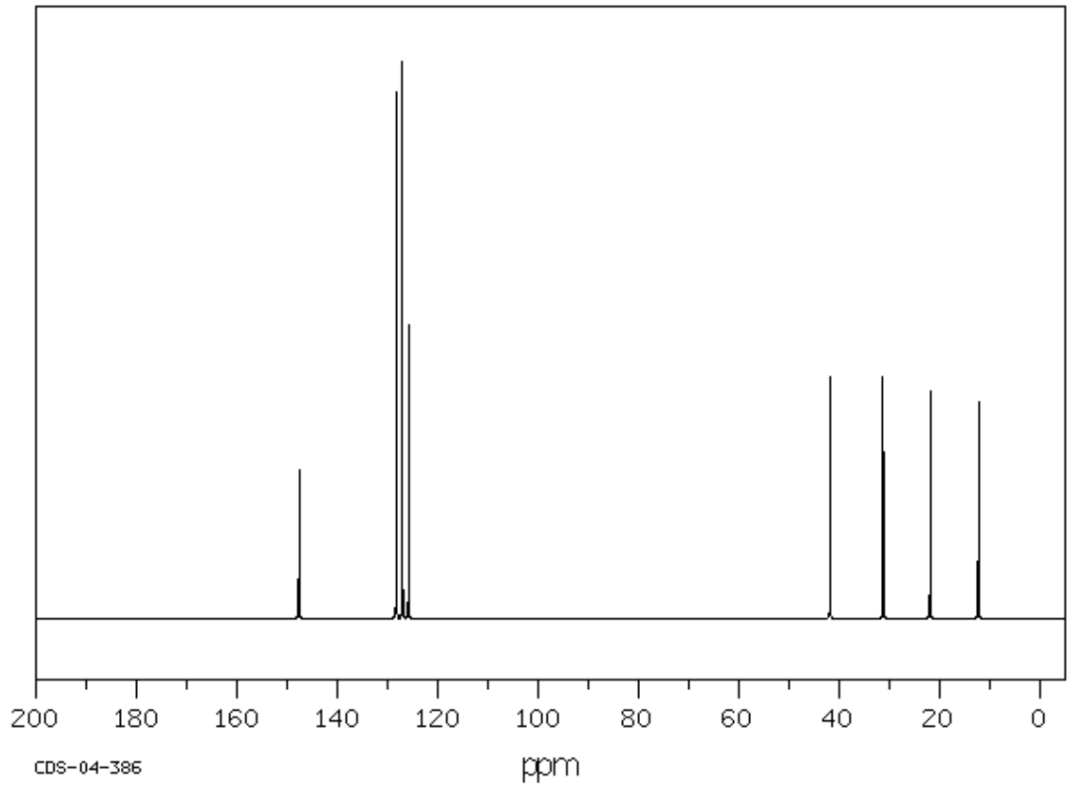


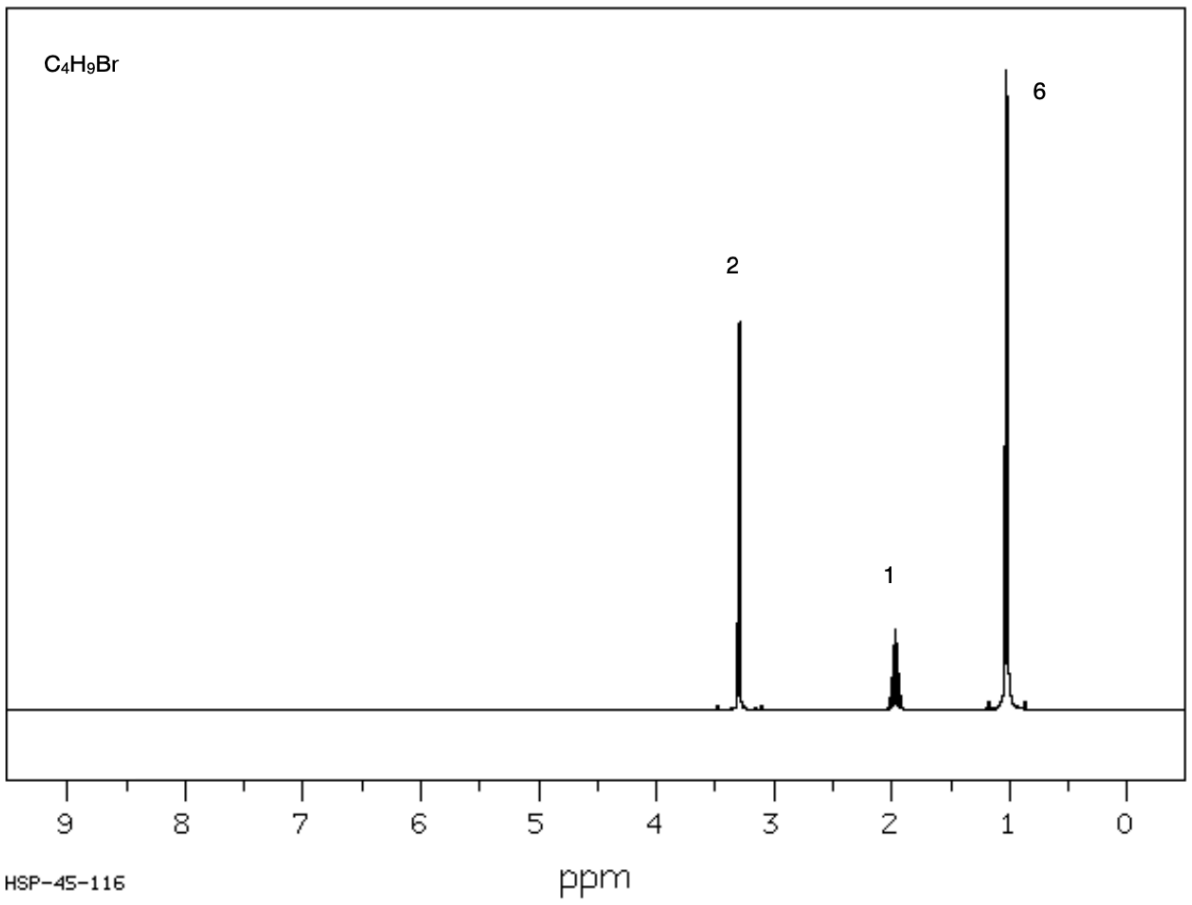


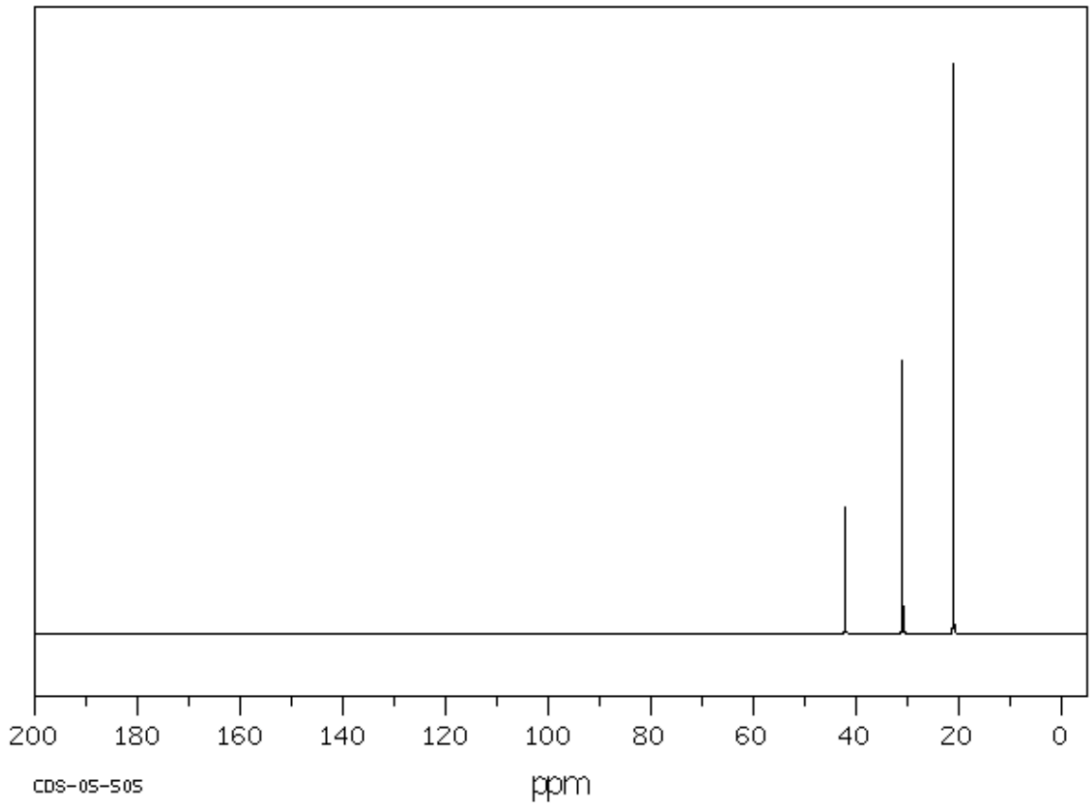










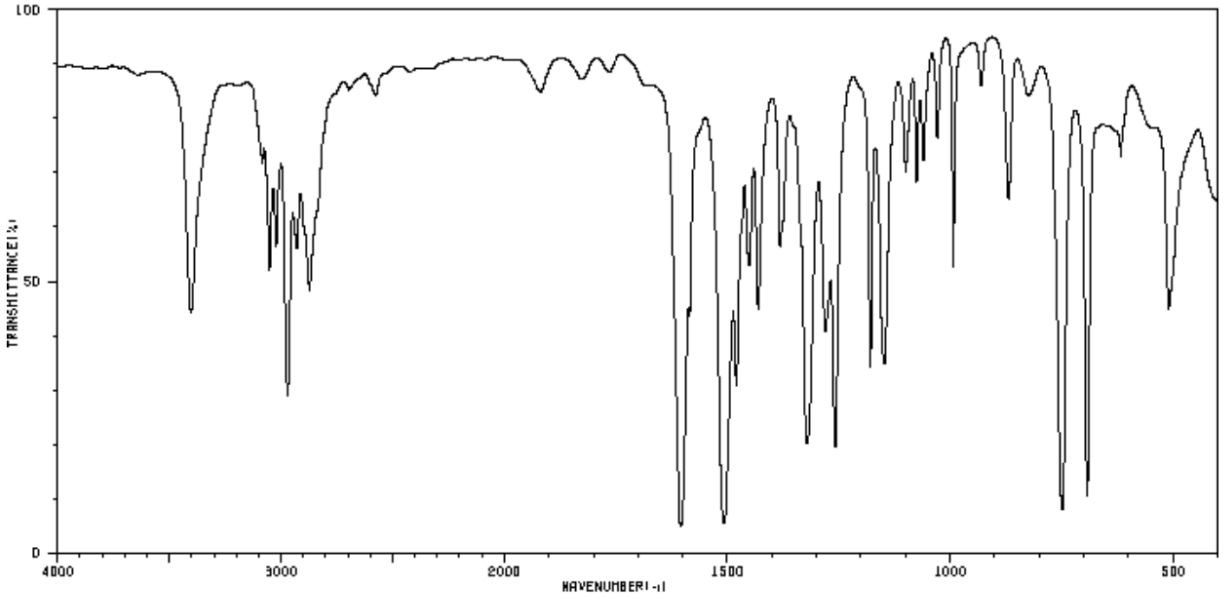


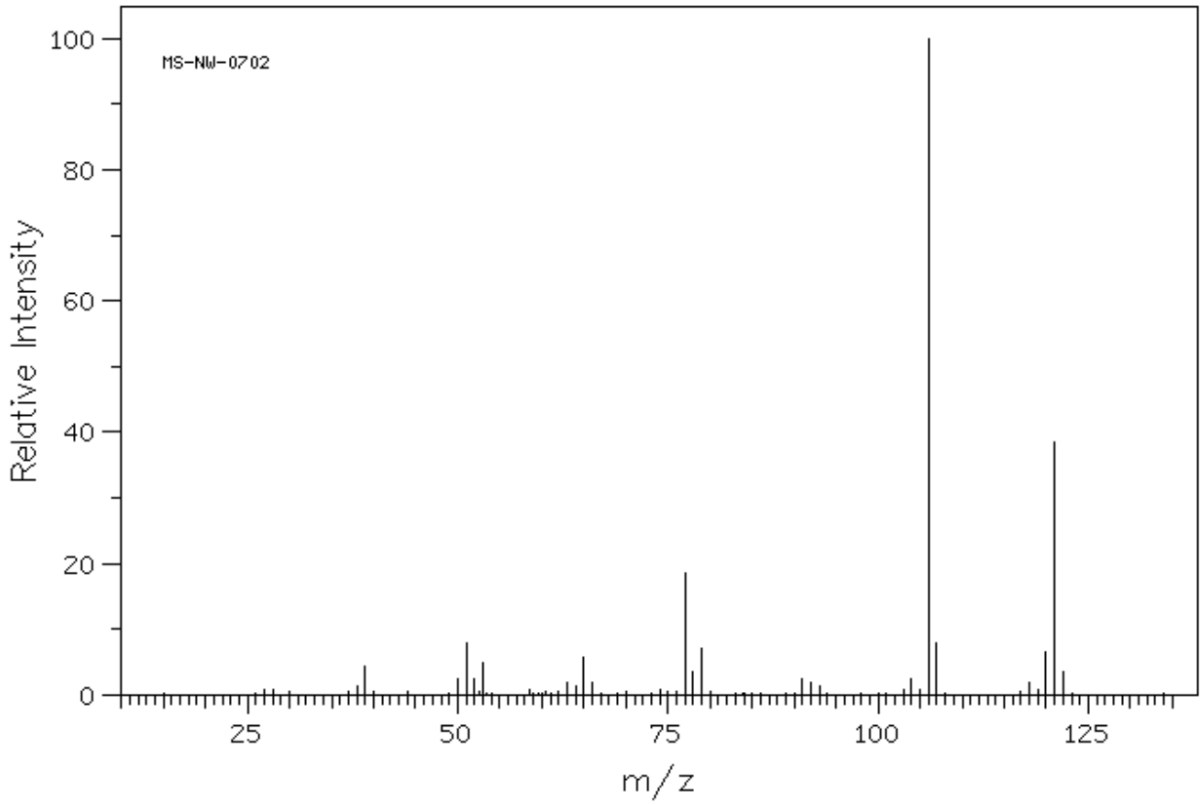
30: COMBINED SPECTRA SETS: IR, MS, ^{1}H-NMR, AND ^{13}C-NMR

Each set of spectra (IR, MS, ^{1}H-NMR, and ^{13}C-NMR) correspond to the same molecule. Determine the structure of each molecule. Follow these steps in your analyses:

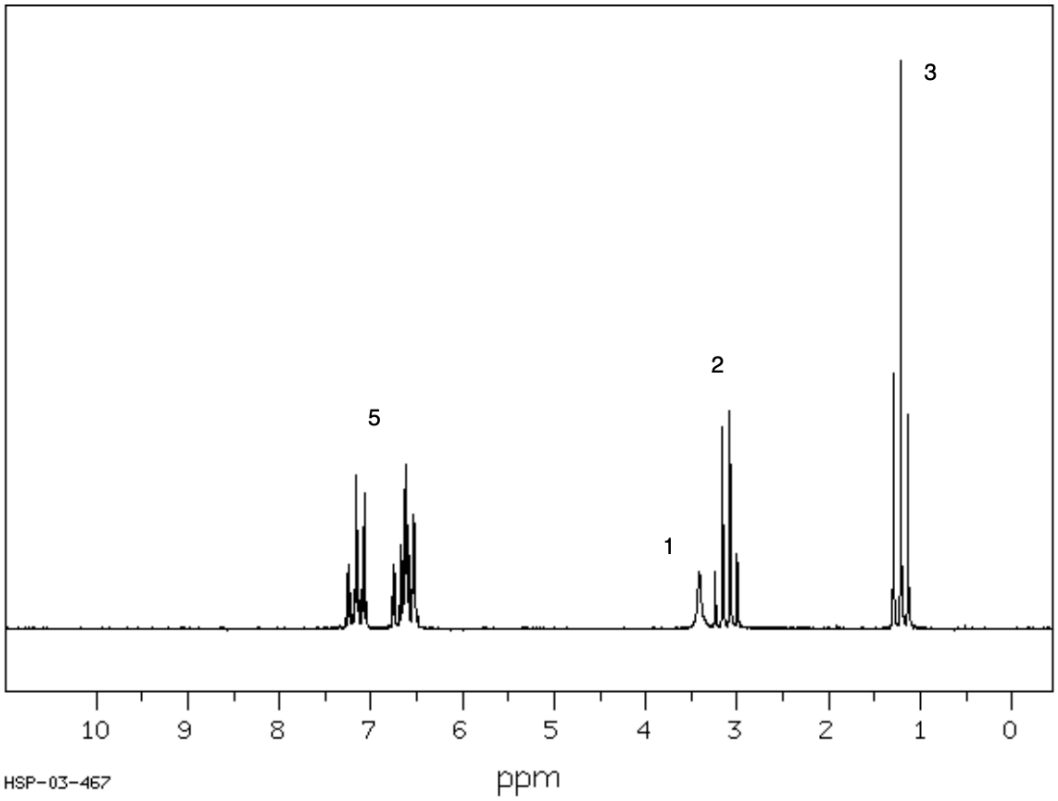
1. Use MS to determine the molecular weight
2. Use MS to determine if there are any N, Cl, or Br atoms present
3. Use IR to determine if there are any O atoms present
4. Use the Rule of 13 to calculate the molecular formula
5. Calculate the HDI
6. Use the IR and ^{1}H-NMR to determine which functional groups are present
7. Analyze the ^{1}H-NMR integration and compare to the molecular formula to make sure the integration is correct
8. Analyze the number of ^{13}C peaks and compare to the molecular formula to get information about the symmetry of the molecule
9. Draw a molecular fragment that is consistent with the ^{1}H-NMR splitting of each peak
10. Combine the fragments into a molecule

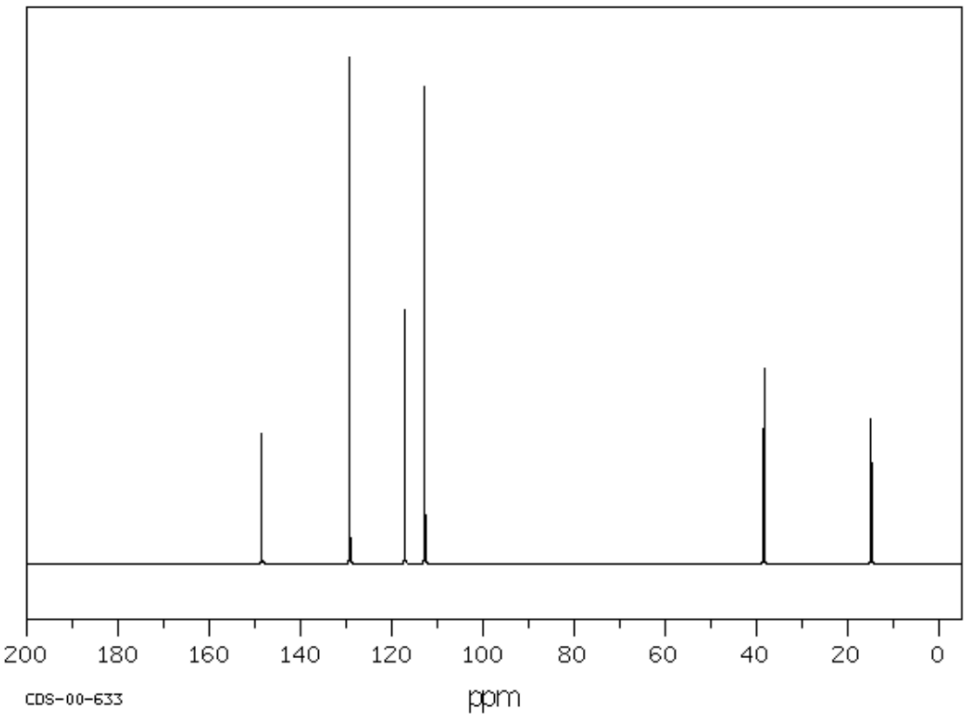
Molecule 1: IR and MS



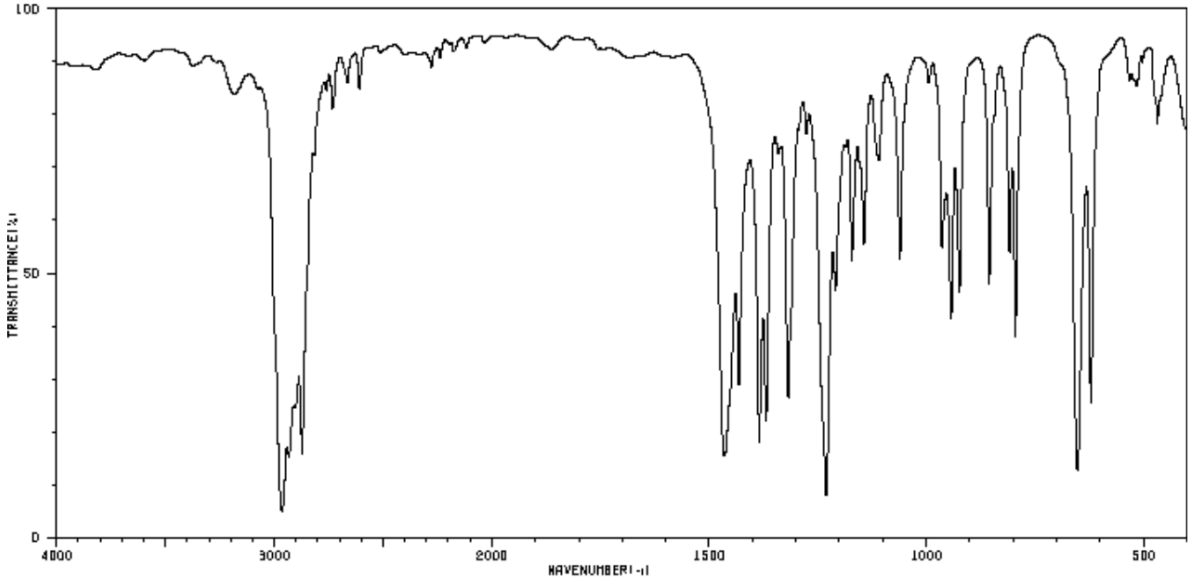


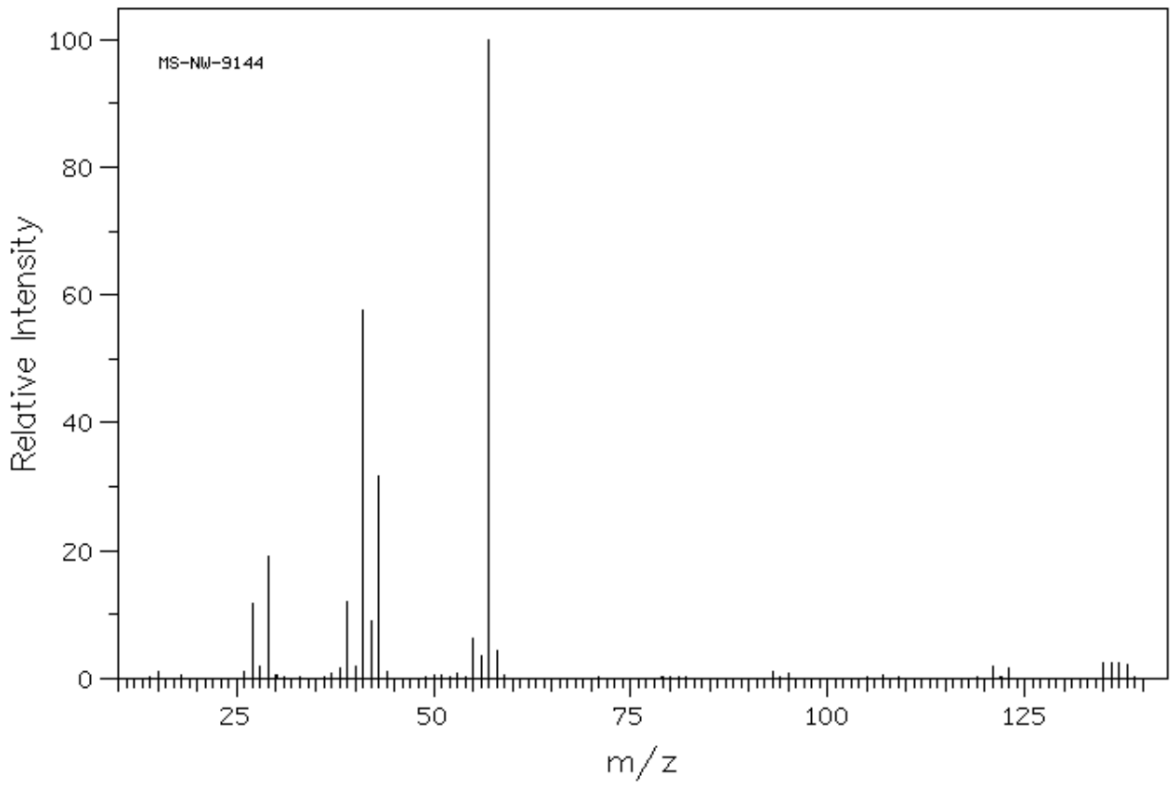
Molecule 1: ^{1}H-NMR and ^{13}C-NMR



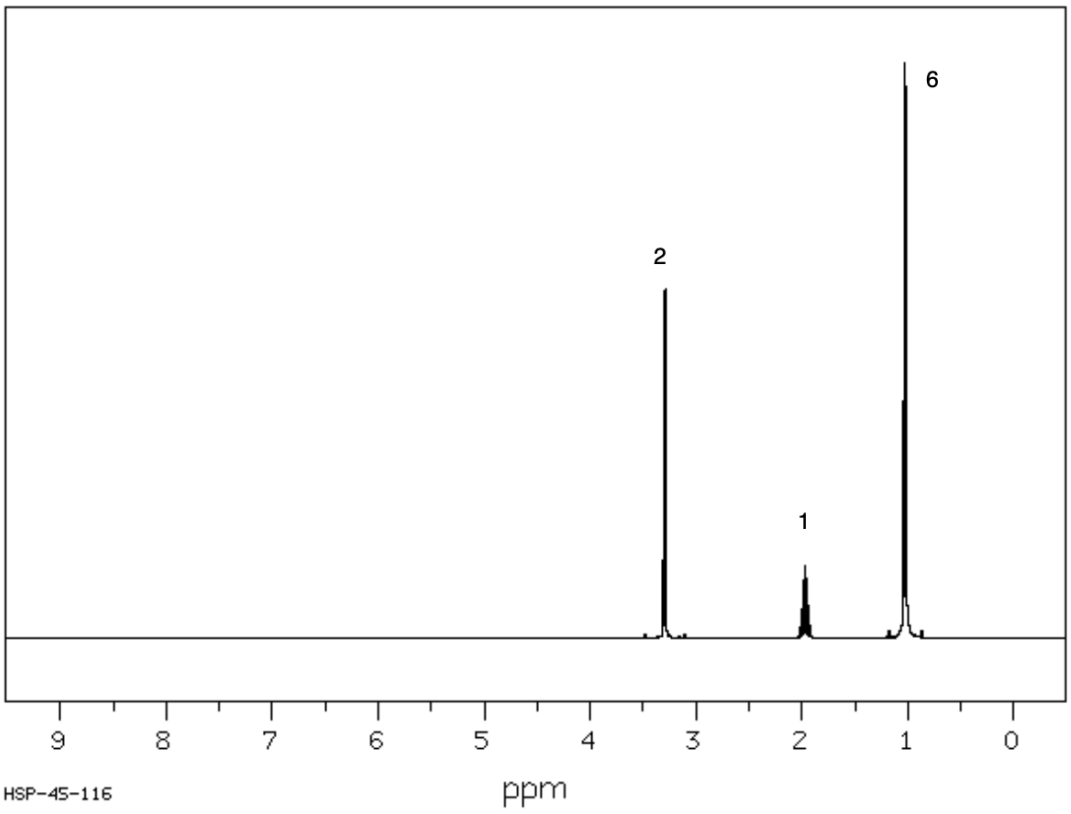


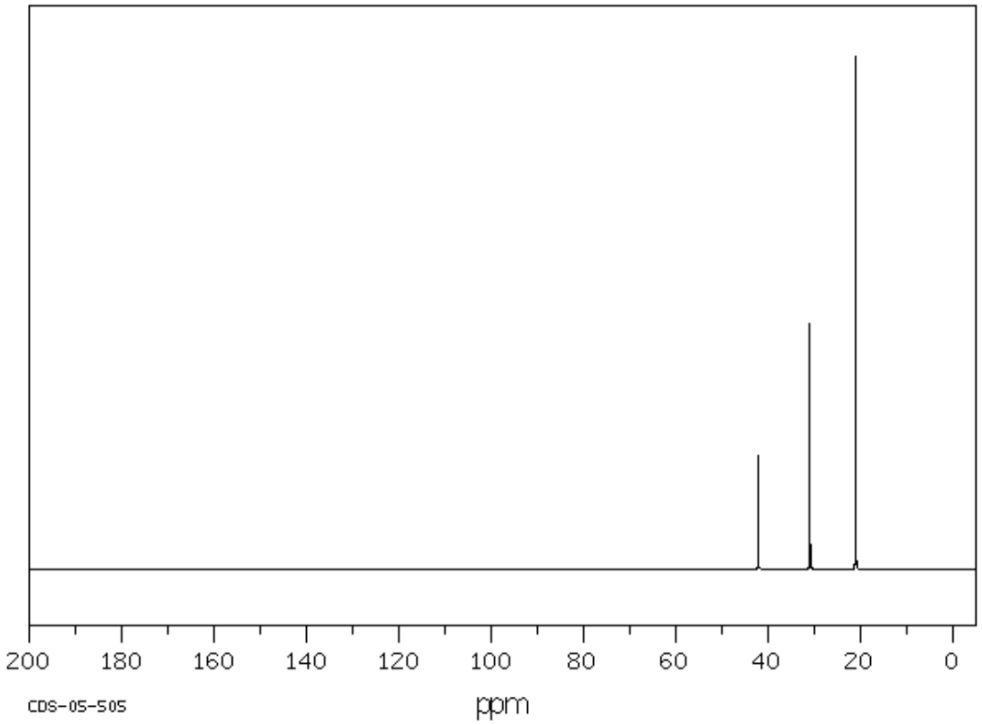
Molecule 2: IR and MS



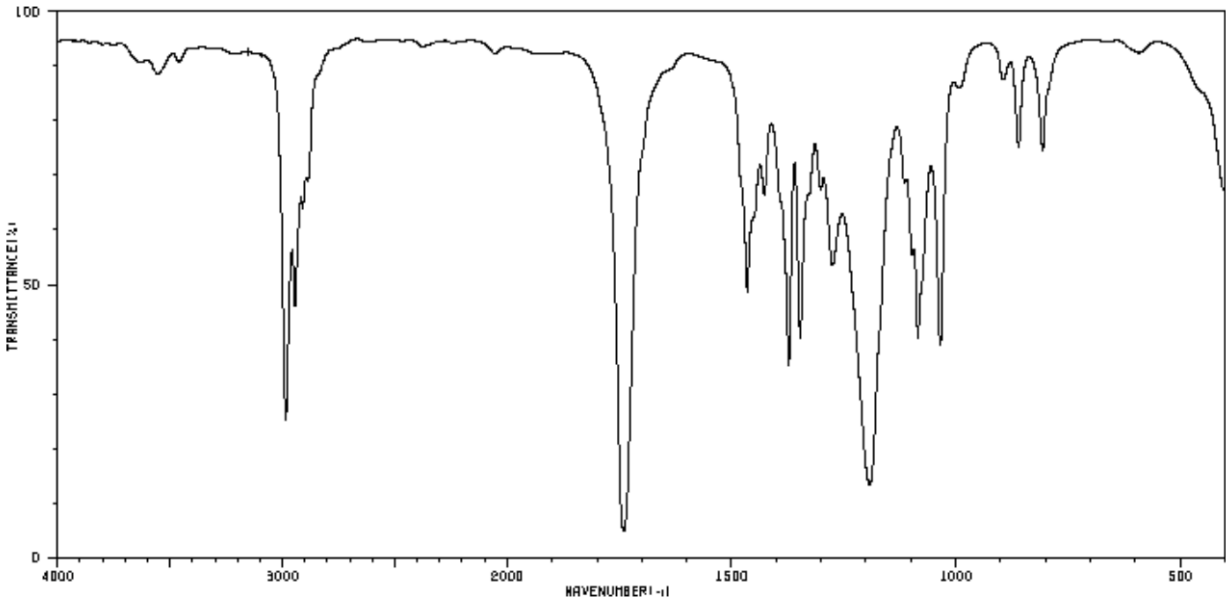


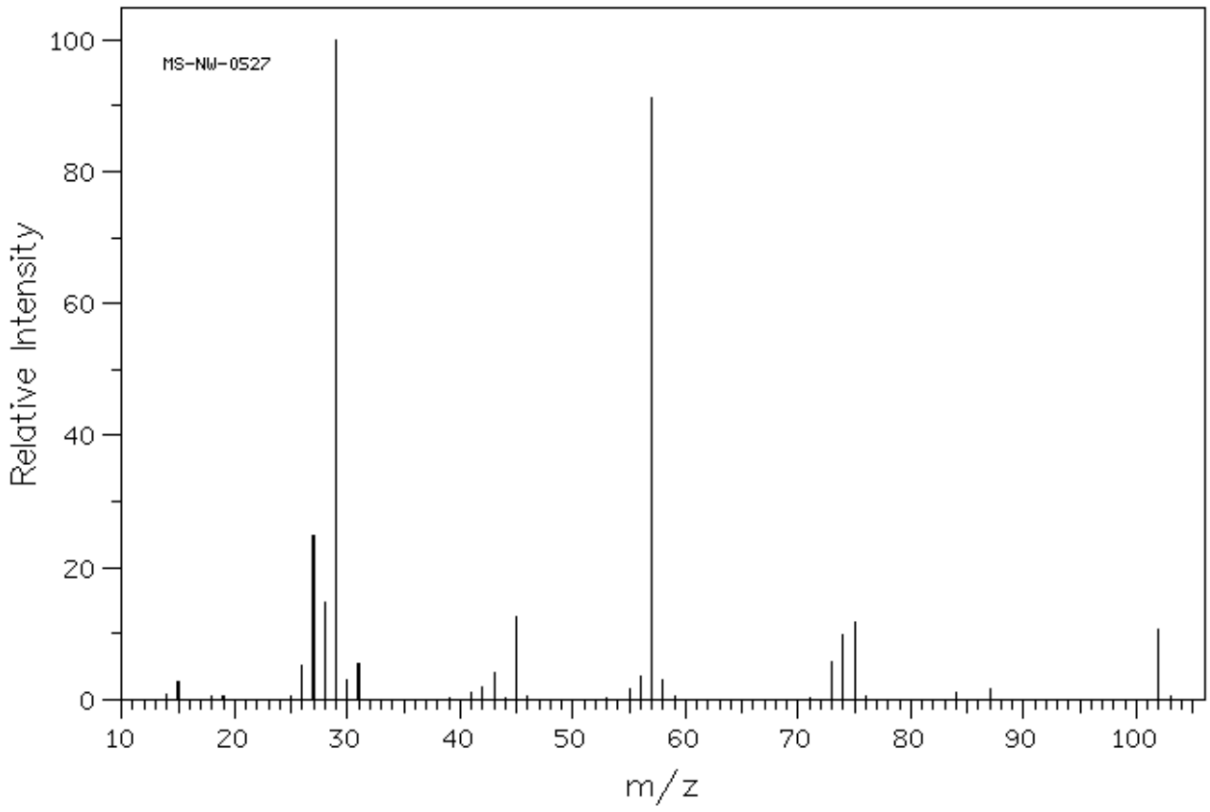
Molecule 2: ^{1}H-NMR and ^{13}C-NMR



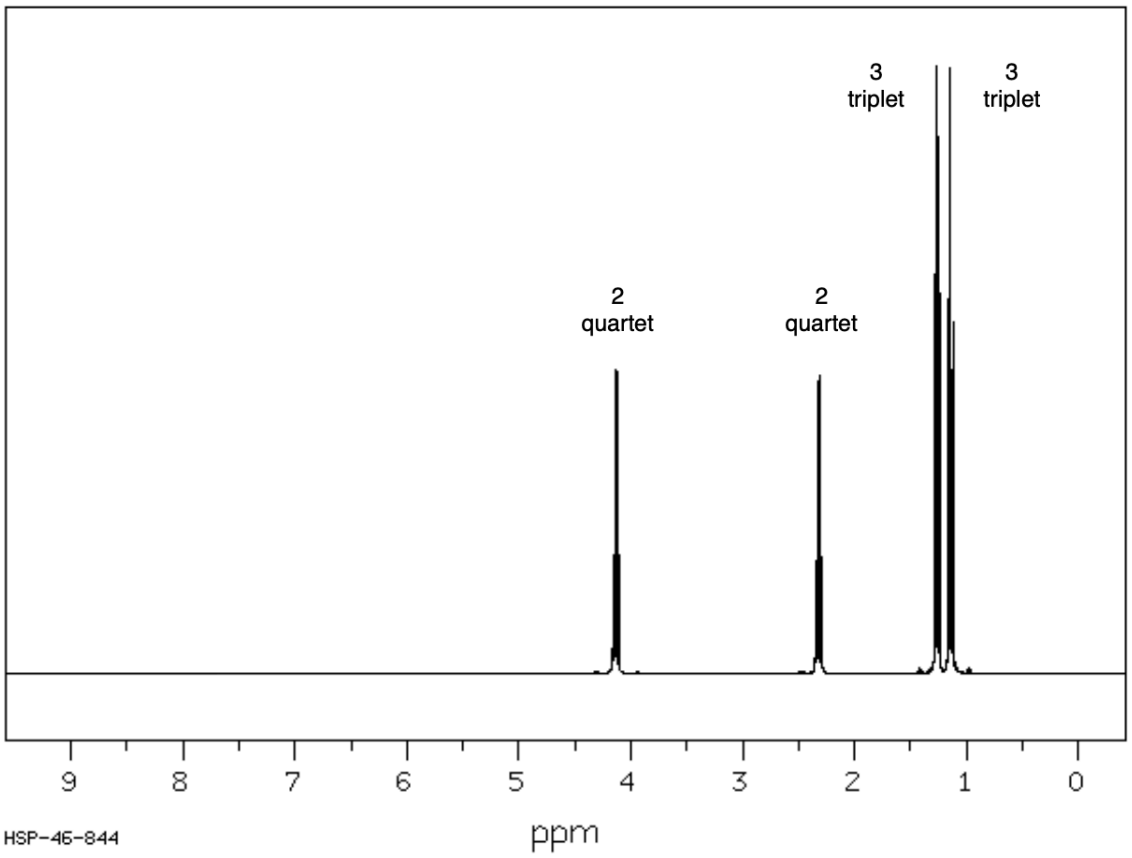


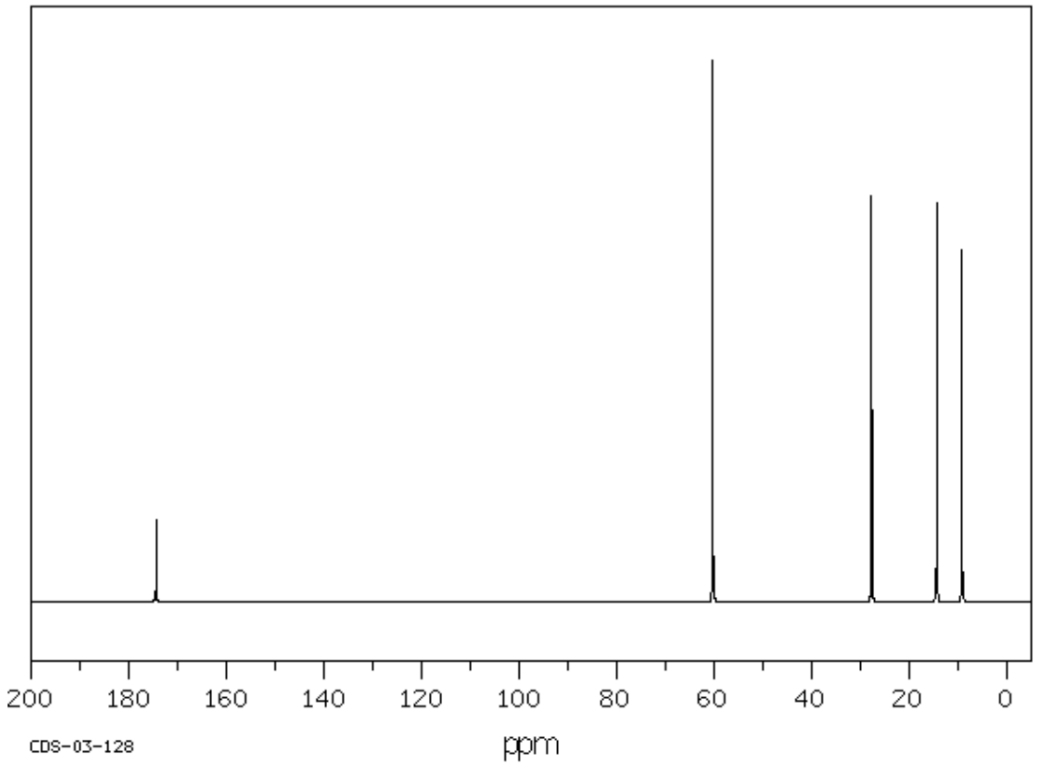
Molecule 3: IR and MS



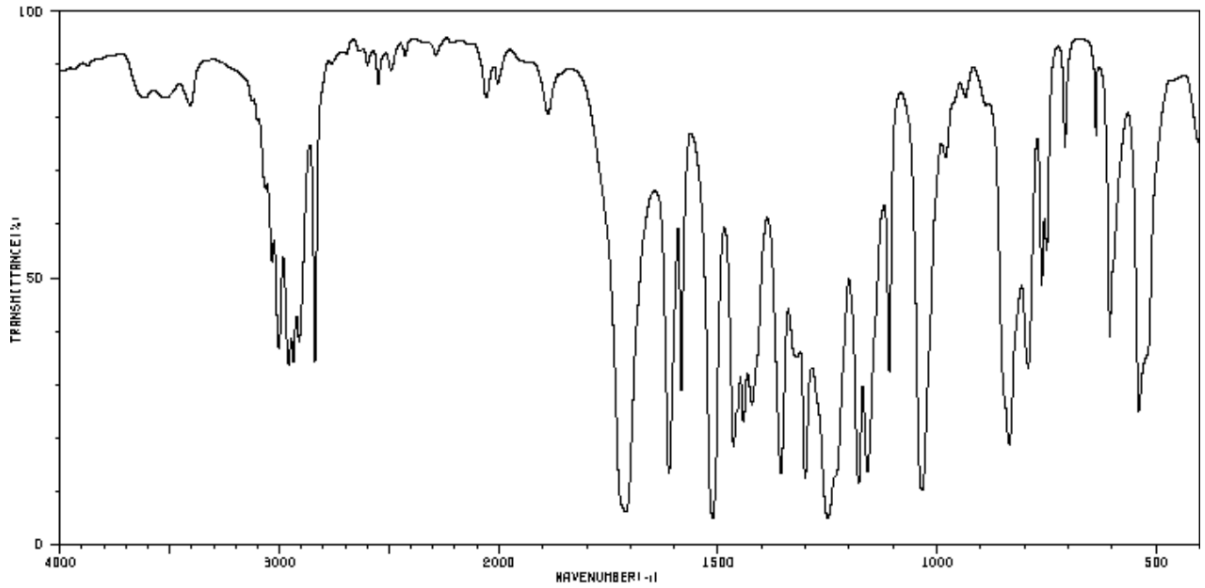


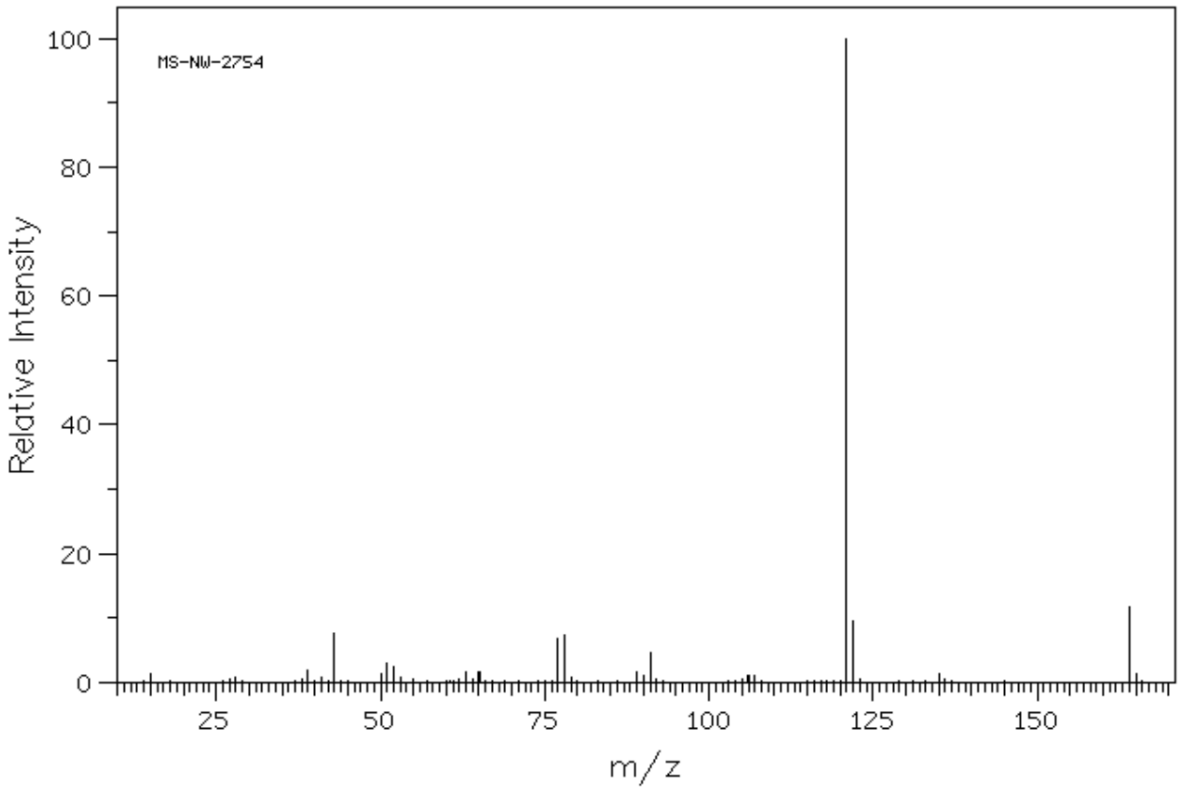
Molecule 3: ^{1}H-NMR and ^{13}C-NMR



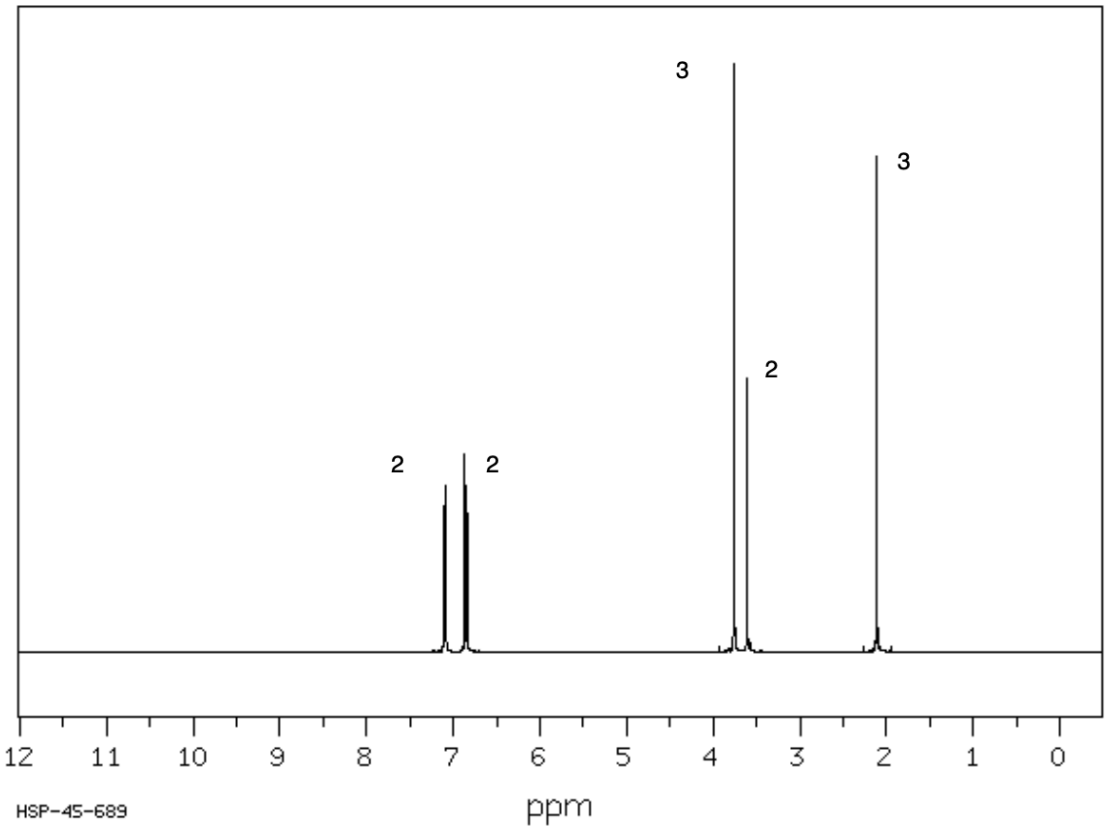


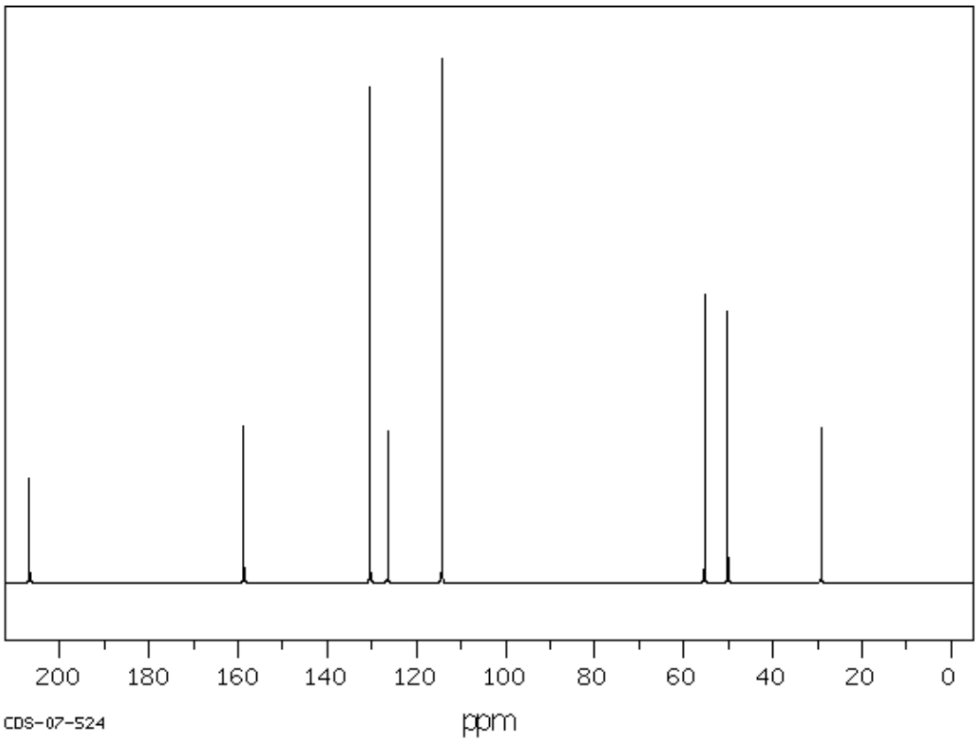
Molecule 4: IR and MS





Molecule 4: ^{1}H-NMR and ^{13}C-NMR





16: CONJUGATED PI SYSTEMS AND PERICYCLIC REACTIONS

MAIN IDEA

A *diene* is a molecule that contains two carbon-carbon double bonds. When these double bonds are separated by only one single bond, the bonds are referred to as *conjugated.* Conjugated double bonds are exceptionally stable due to the extensive delocalization of electrons through the adjacent p orbitals of the double bonds. This usual stability causes conjugated dienes to undergo different reactions than those of regular alkenes.

OBJECTIVES

- Learn the difference between conjugated, cumulated, and isolated dienes
- Understand what contributes to the stability of different types of dienes
- Learn how temperature affects the addition of HX and Br_2 to a diene
- Learn the Diels-Alder reaction
- Understand how and why sigmatropic rearrangements occur

SKILLS TO MASTER

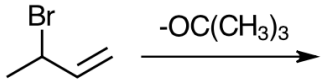
- Predict the relative stability of conjugated, cumulated, and isolated dienes
- Draw the mechanisms for the following reactions:
    - Addition of HX to a diene at different temperatures
    - Addition of Br_2 to a diene at different temperatures
    - Diels-Alder
    - Sigmatropic rearrangement
- Select the correct starting molecules to perform a Diels-Alder reaction

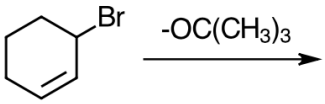
TERMINOLOGY

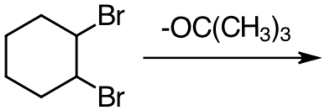
- Conjugated diene
- Cumulated diene
- Diene
- Dienophile
- Isolate diene
- Kinetic control
- *s-cis*
- *s-trans*
- Thermo control

31: CONJUGATED DIENES: SYNTHESIS AND STABILITY

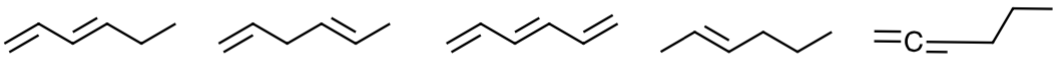
1. Predict the products of the following elimination reactions. The product of each reaction is a conjugated diene. This reaction is usually done with tert-butoxide (“bulky base”) to avoid competition with the SN2 mechanism.



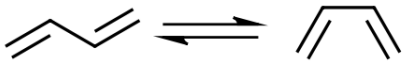




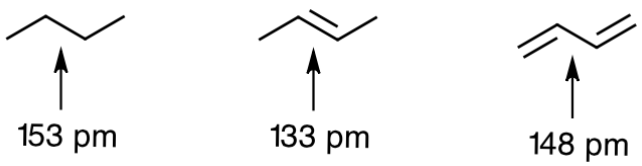
2. Conjugation increases the stability of a molecule. As the conjugation of a molecule increases, so does its stability. Use this information to rank the relative stability of the following molecules.



3. Dienes have free rotation around the C-C single bond that separates the C=C double bonds. The molecule can freely rotate in equilibrium between a *cis-like* conformation and a *trans-like* conformation that we call ***s-cis*** and ***s-trans***. Label the following structures as *s-cis* or *s-trans*. Which conformation is more stable? Does the position of equilibrium lie to the left or to the right?



Observe the trend in carbon-carbon bond length and use it to answer the following questions.



4. What is the hybridization of C#2 and C#3 in butane (the first structure)?

5. What is the hybridization of C#2 and C#3 in 2-butene (the middle structure)?

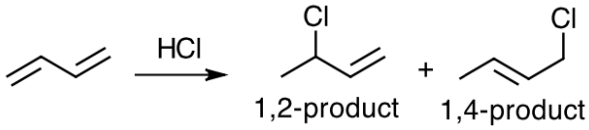
6. Why is the C-C single bond in butane longer than the C=C double bond in 2-butene? (Do not just answer “double bonds are shorter than single bonds”. Explain WHY double bonds are shorter than single bonds.)

7. What is the hybridization of C#2 and C#3 in 1,3-butadiene (the last structure)?

8. Why is the C-C single bond in 1,3-butadiene shorter than the C-C single bond in butane?

32: ELECTROPHILIC ADDITION TO DIENES

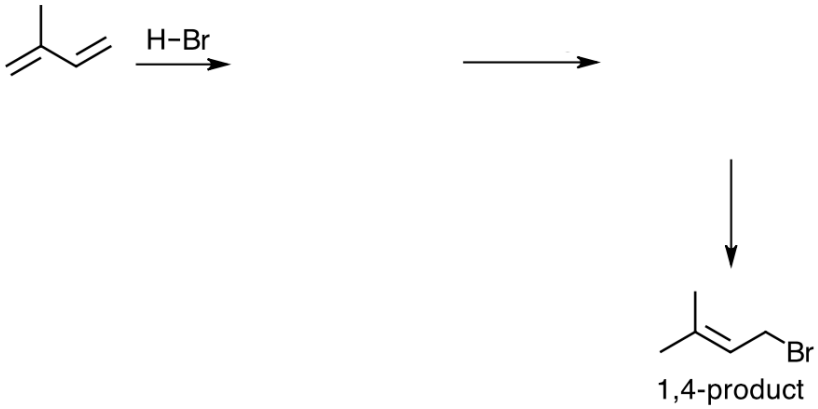
1. Dienes undergo addition reactions similar to those of alkenes. For example:



   - This reaction works with HCl, HBr, and Br_2.
   - The product on the left is called a **1,2-product** because HCl was added to the first and second carbons of the diene. (These numbers rarely correspond to the IUPAC numbering system for the molecule. They correspond only to the 4 carbons of the conjugated diene.)
   - The product on the right is called a **1,4-product** because HCl was added to the first and fourth carbons of the diene.

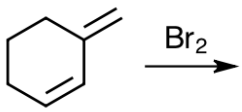
2. Propose a mechanism that accounts for the formation of the 1,2-product. This product is formed by a standard addition reaction.

3. Propose a mechanism that accounts for the formation of the 1,4-product. This product is formed from a resonance structure of the carbocation intermediate. This resonance structure will make you uncomfortable. Proceed anyway, and find the resonance structure that will allow you to form the 1,4-product.



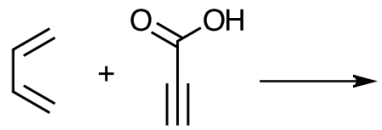
4. As you just observed, the mechanism for the formation of the 1,4-product involves addition to the least-stable resonance structure. Propose an explanation for this. (*Hint: Compare the stability of the 1,2- and 1,4-products*.)

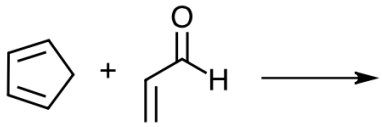
5. Draw and label the 1,2- and 1,4-products of the following reaction:

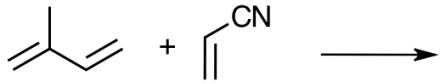


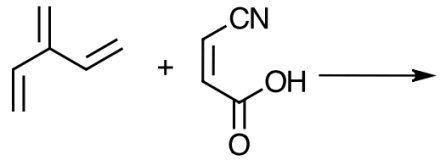
33: DIELS-ALDER REACTION

1. Predict the products of the following Diels-Alder reactions.

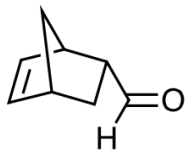


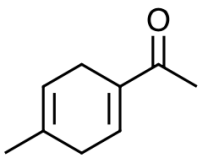






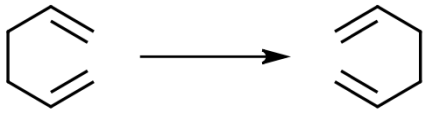
2. Show how to make the following molecules via a Diels-Alder reaction.



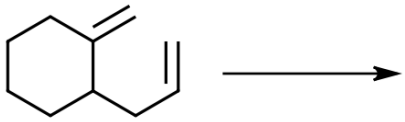


34: SIGMATROPIC REARRANGEMENTS

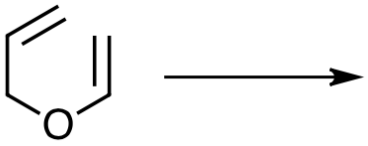
1. A sigmatropic rearrangement resembles a Diels-Alder reaction. It is an intramolecular (within one molecule) rearrangement. The following reaction is an example of a sigmatropic reaction. Draw three curved arrows on the reactant to show the formation of the product.



2. When the rearranging portion of the molecule contains only carbon atoms, the reaction is called a Cope Rearrangement. Draw curved arrows and predict the product of the following reaction.



3. When the rearranging portion of the molecule contains one oxygen atom, the reaction is called a Claisen Rearrangement. Draw curved arrows and predict the product of the following reaction.



4. What is the motivation for a sigmatropic rearrangement? Why do they proceed?

17: AROMATIC COMPOUNDS

MAIN IDEA

Cyclic conjugated pi systems display either significant stability or significant instability, depending on the number of electrons in the conjugated pi system. This stability or instability extends to heterocycles (molecules that have atoms other than carbon in the ring) as well as cyclic molecules that are not fully conjugated, but still have similar properties due to formal charges or lone pairs of electrons on the atoms of the ring.

OBJECTIVES

- Learn the IUPAC system of naming substituted benzene rings
- Understand Hückel's Rule and learn how to apply it to cyclic molecules
- Understand the reactivity of benzylic carbon atoms
- Learn how to convert benzene to a non-aromatic molecule

SKILLS TO MASTER

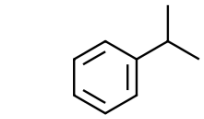
- Name substituted benzene rings using both numbers and prefixes to locate substituents
- Classify molecules as aromatic, anti-aromatic, or non-aromatic
- Draw the products for the following reactions:
    - Side-chain oxidation
    - Catalytic reduction of benzene
    - Birch reduction of benzene
- Identify the reagents needed for the following reactions:
    - Side-chain oxidation
    - Catalytic reduction of benzene
    - Birch reduction of benzene

TERMINOLOGY

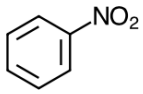
- Anti-aromatic
- Aromatic
- Benzylic
- Heterocyclic
- Hückel’s Rule
- Kekulé structure
- Meta
- Non-aromatic
- Ortho
- Para
- Phenyl

35: NOMENCLATURE OF SUBSTITUTED BENZENE

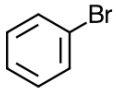
1. When a benzene ring has only one substituent, name it as a substituted benzene. Look at the two examples and then provide names for the other two monosubstituted benzenes.

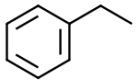


isopropylbenzene

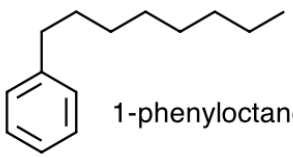


nitrobenzene

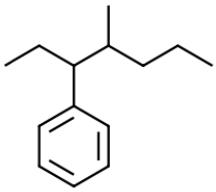




2. If the substituent is the longest carbon chain in the molecule (7 or more carbons), you must name the benzene ring as a substituent on the carbon chain. Benzene as a substituent is called “phenyl”. Look at the following example and then name the other compound.

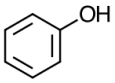


1-phenyloctane

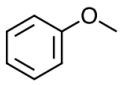


3. There are 9 substituted benzene rings that are known by specific names. Memorize all 9 of these benzene derivatives and their names.

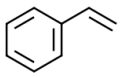
toluene



phenol

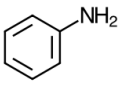


anisole

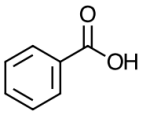


styrene

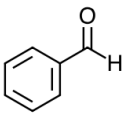
xylene
(the two methyl groups can be located anywhere on the ring)



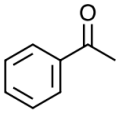
aniline



benzoic acid

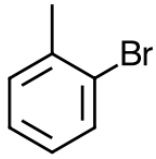


benzaldehyde

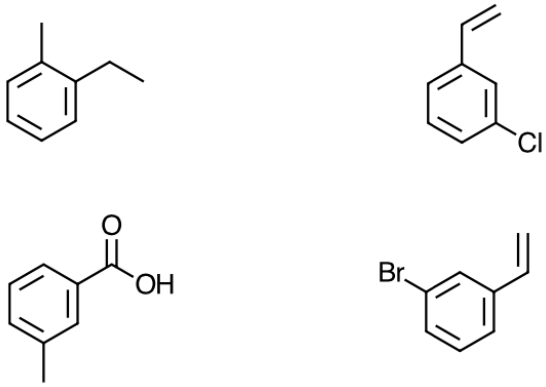


acetophenone

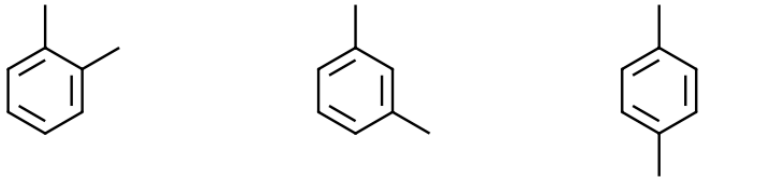
4. If there is another substituent on one of the 9 benzene derivatives, it is named as a substituted version of that derivative. For example, this compound is named as 2-bromotoluene. (Because the methyl group is what makes the compound toluene, the carbon holding the methyl group is given #1.) This molecule would not normally be named as 1-bromo-2-methylbenzene, although that name is logical and interpretable.



5. Practice naming the following disubstituted benzene rings.



6. The location of the substituents on a disubstituted benzene ring can also be described using prefixes ortho-, meta-, and para-, abbreviated (o)-, (m)-, and (p)-. Look at the following examples, then re-name the molecules in problem 5 using the ortho-, meta-, and para- prefixes.



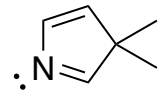
1,2-xylene
o-xylene
(pronounced:
ortho xylene)

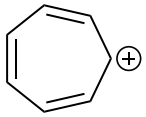
1,3-xylene
m-xylene
(pronounced:
meta xylene)

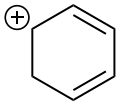
1,4-xylene
p-xylene
(pronounced:
para xylene)

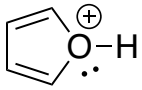
36: AROMATIC COMPOUNDS

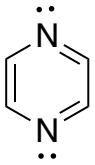
Classify each molecule as aromatic, anti-aromatic, or non-aromatic.

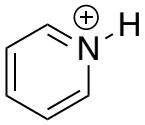






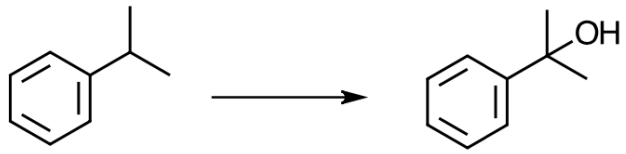


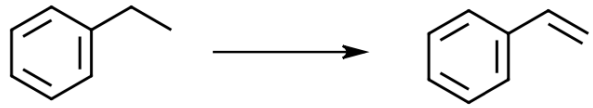


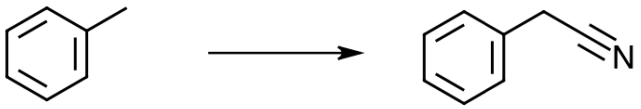


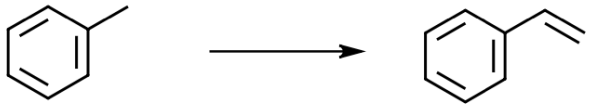
37: REACTIONS AT THE BENZYLIC POSITION

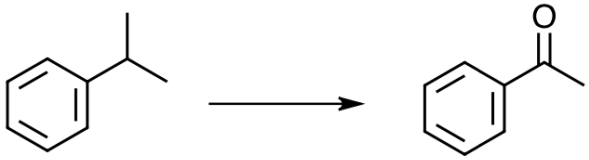
Show how to perform each of the following reactions.

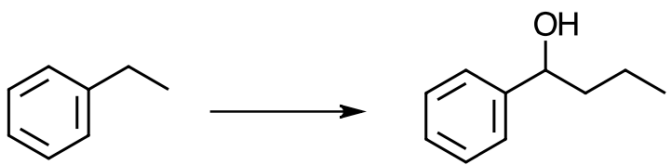






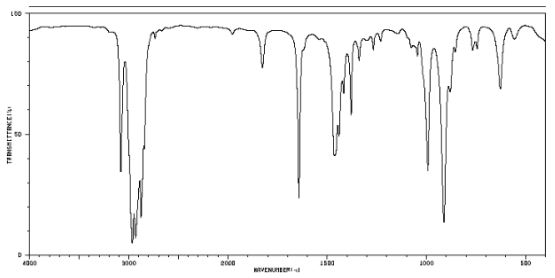


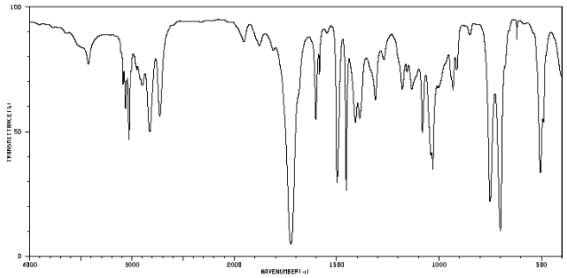


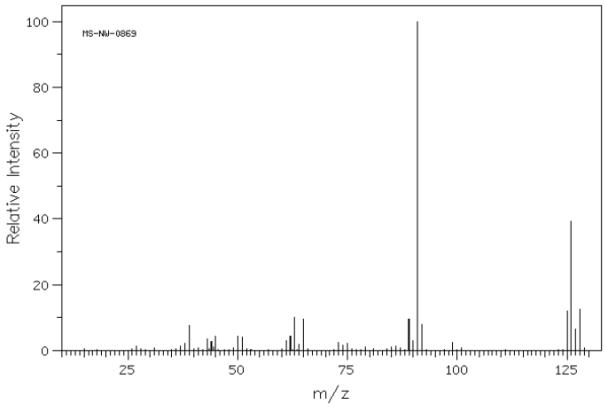


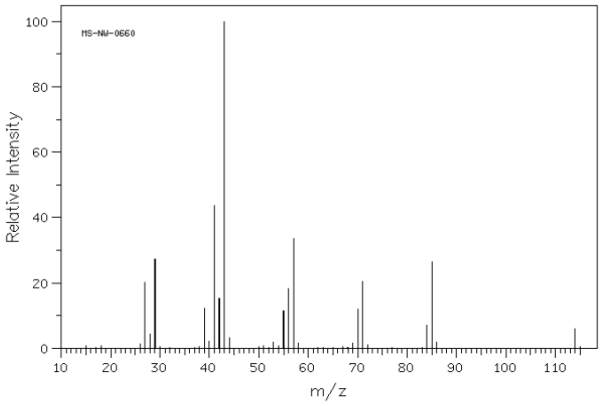
38: SPECTROSCOPY OF BENZENE DERIVATIVES

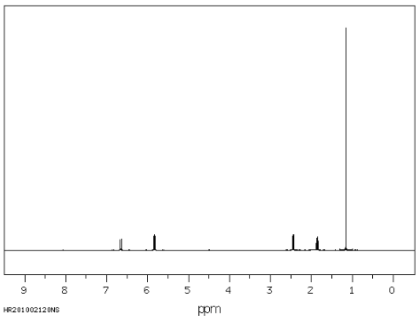
For each pair of spectra, identify which one represents a molecule containing a benzene ring. Do not attempt to determine the structures of the molecules.

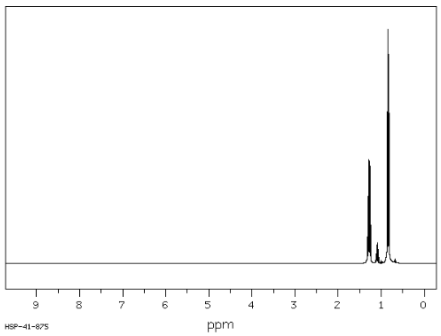


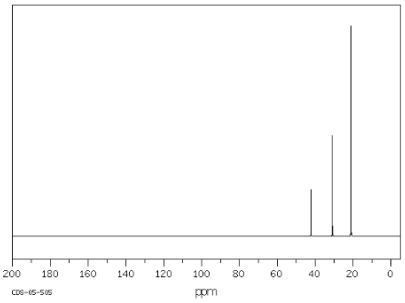


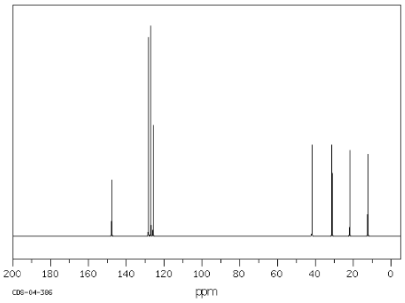












18: AROMATIC SUBSTITUTION REACTIONS

MAIN IDEA

The carbon atoms of benzene and its derivatives can undergo both electrophilic and nucleophilic substitution reactions. Electrophilic aromatic substitution involves the substitution of a hydrogen atom with a new substituent. All existing substituents on the benzene ring will affect the rate of this reaction, with some causing the reaction to proceed at a faster rate and others causing the rate of the reaction to decrease. In addition, existing substituents on the benzene ring will influence which hydrogen atom undergoes electrophilic aromatic substitution, and therefore will ultimately determine the location of the new substituent. Nucleophilic aromatic substitution reactions involve the substitution of a more traditional leaving group with a new substituent. These reactions are comparable to S_N1 and S_N2 mechanisms.

OBJECTIVES

- Understand electrophilic and nucleophilic aromatic substitution reactions
- Learn how existing substituents affect aromatic substitution reactions

SKILLS TO MASTER

- Classify substituents on a benzene ring as either activating or deactivating
- Classify substituents on a benzene ring as either ortho-/para-directing or meta-directing
- Know the necessary reagents, draw the mechanism, and predict the products for the following reactions involving benzene and benzene derivatives:
    - Halogenation
    - Sulfonation
    - Nitration
    - Friedel-Crafts alkylation
    - Friedel-Crafts acylation
    - Nucleophilic aromatic substitution
    - Elimination-addition (“benzyne” reaction)

TERMINOLOGY

- Activating group
- Benzyne
- Deactivating group
- Sigma complex

39: ELECTROPHILIC AROMATIC SUBSTITUTION

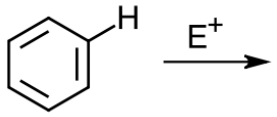
1. Propose a general mechanism for electrophilic aromatic substitution using the benzene ring drawn below. Use the following steps as your guide.

    1. Begin by attacking the electrophile (E+) with a double bond. (Choose the double bond associated with the “shown” hydrogen.)

    2. Add the electrophile to the same carbon as the one with the shown hydrogen. Your intermediate will have a positive formal charge.

    3. Draw two resonance structures for your intermediate. All three representations of your intermediate are collectively called the sigma complex. Is the sigma complex aromatic?

    4. Use a base (just write “base”) to abstract the shown hydrogen. Return the C-H electrons into the ring and restore the molecule’s aromaticity.

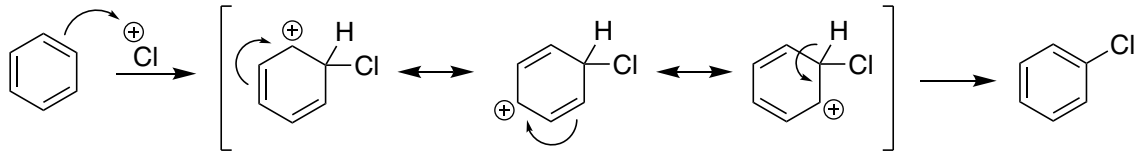


2. Draw the mechanism for the chlorination of benzene. Use the above mechanism as your guide. The electrophile is Cl^+ and the base is $AlCl_4^-$.

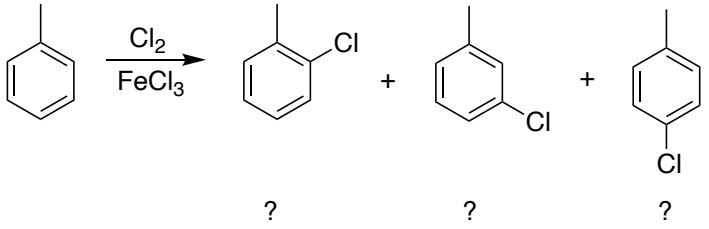
3. Draw the mechanism for the Friedel-Crafts alkylation of benzene. Use 1-chloropropane as your alkyl halide. Pay attention to the structure of your carbocation electrophile. The base is $AlCl_4^-$.

40: ACTIVATING, DEACTIVATING, AND DIRECTING SUBSTITUENTS

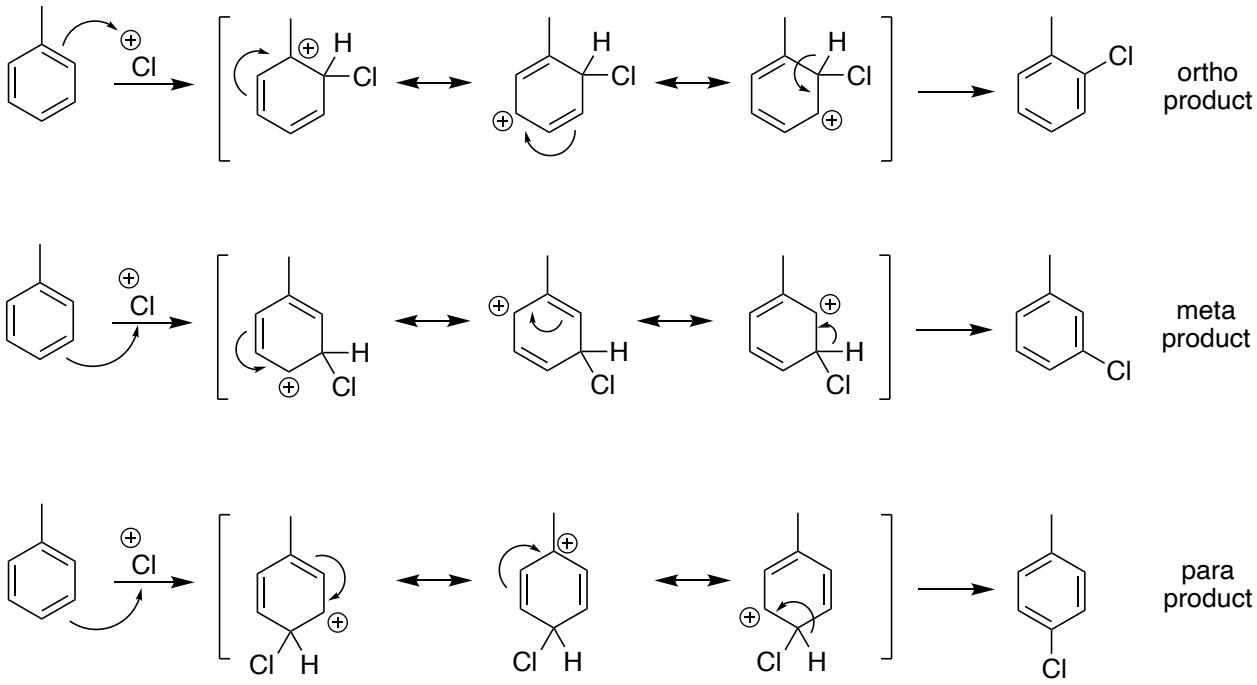
Review the mechanism for the chlorination of benzene:



How would this reaction be different if the benzene ring already had a substituent? For example, consider the chlorination of toluene. Where will the chlorine go, relative to the methyl group? Will the methyl group help reaction proceed faster, or will it slow the reaction down?



To answer these questions, we will study the mechanisms for the formation of the three possible products.



1. Of the three possible mechanisms for the chlorination of toluene (previous page), two mechanisms have something in common. Which two mechanisms are similar, and what do they have in common?

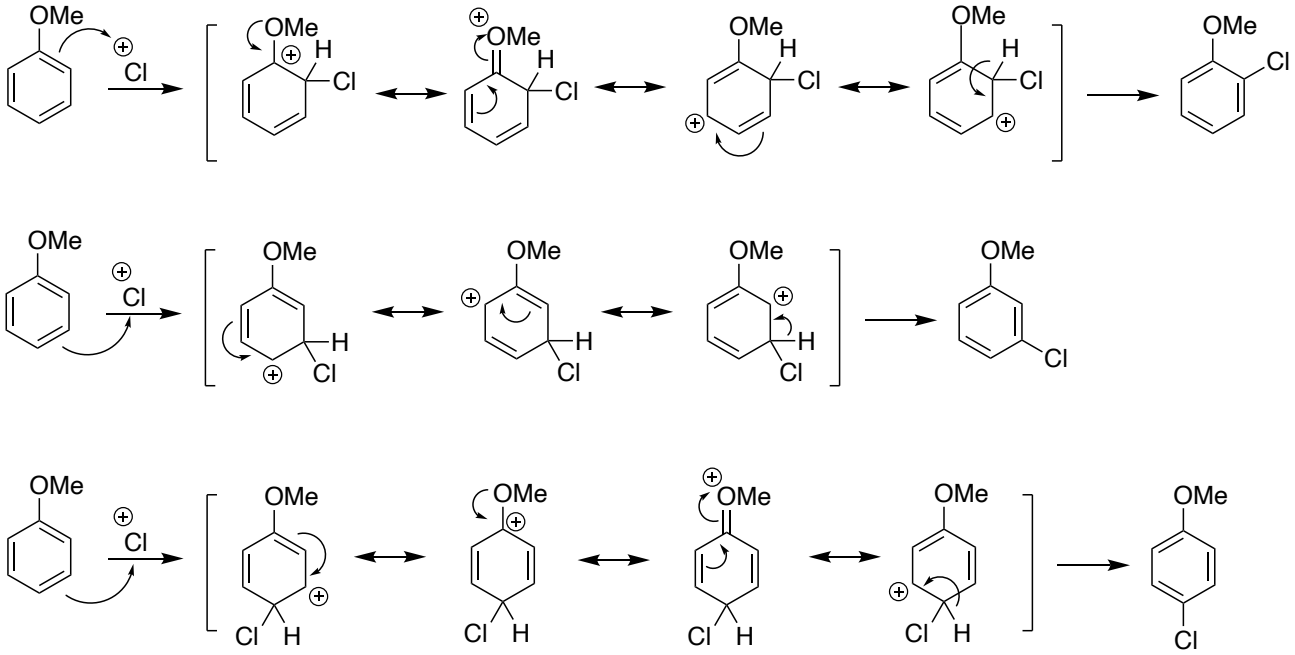
2. Of the three mechanisms, which is/are more thermodynamically favorable? Which is/are less favorable?

3. Do your answers to questions 1 and 2 depend on the electrophile? For example, if we were studying the nitration of toluene, would your answers to problems 1 and 2 be different?

4. If you add a second substituent to an alkylated benzene ring, such as toluene, where will the new substituent be located?

5. If you add a second substituent to an alkylated benzene ring, will that reaction be faster or slower than adding a substituent to the benzene molecule with no substituents?

How would this reaction be different if the existing substituent was something other than a methyl group? Consider the chlorination of anisole.



6. Of the three possible mechanisms above, which two mechanisms are similar, and what do they have in common?

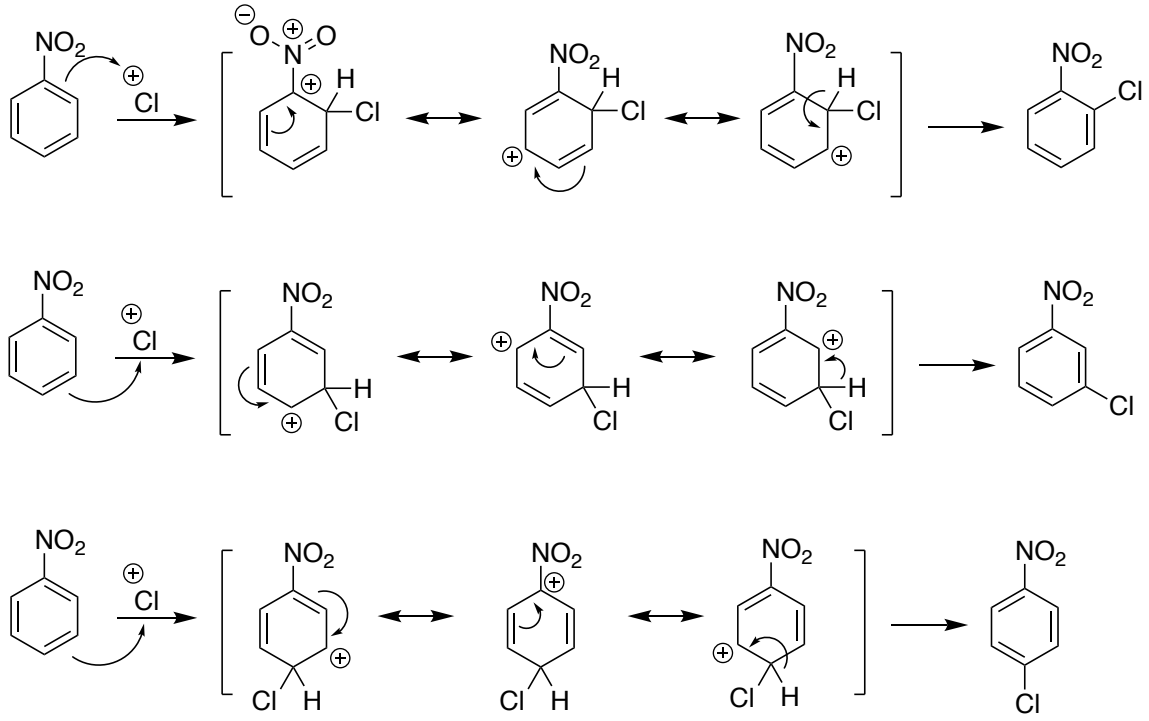
7. Of the three mechanisms, which is/are more thermodynamically favorable? Which is/are less favorable?

8. Do your answers to questions 1 and 2 depend on the electrophile?

9. If you add a second substituent to a benzene ring with an alkoxy group, such as methoxy, where will the new substituent be located?

10. If you add a second substituent to a benzene ring with an alkoxy group, will that reaction be faster or slower than adding a substituent to the benzene molecule with no substituents?

Now we will consider the chlorination of nitrobenzene. One of the nitro groups has been expanded to show you the formal charges on the nitrogen and oxygen. The remaining nitro groups have not been expanded, but they have the same formal charges.



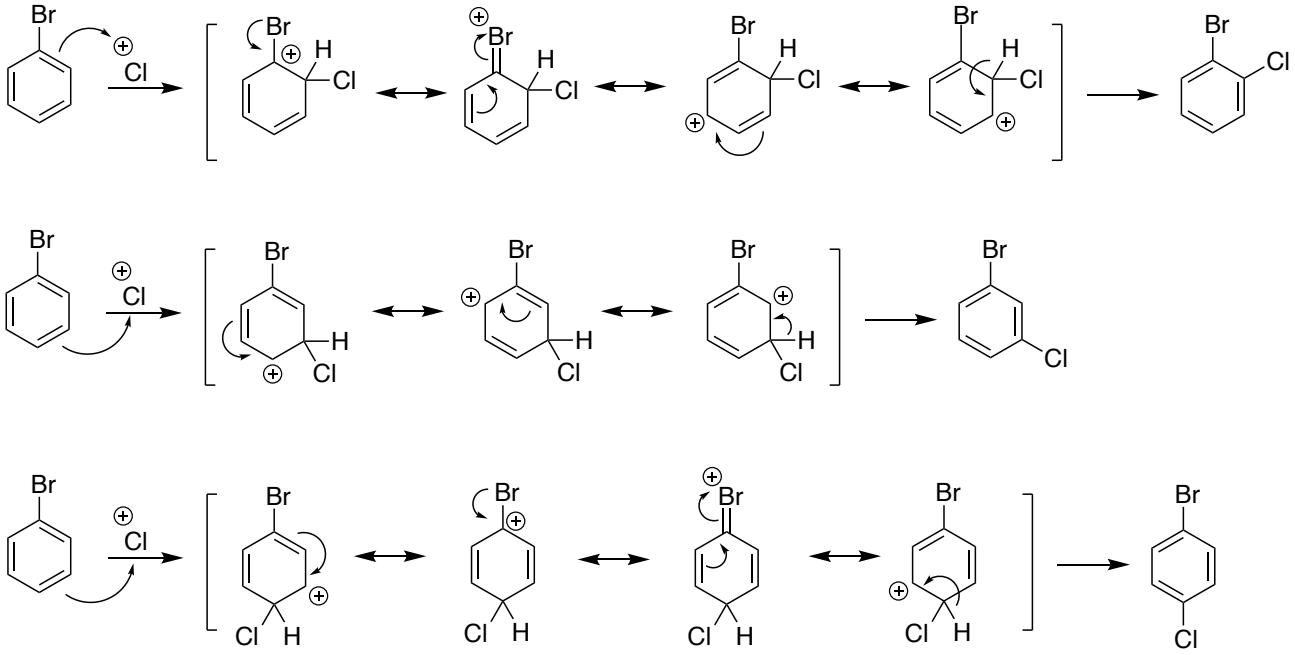
11. Which two of the above mechanisms are similar, and what do they have in common?

12. If you add a second substituent to a benzene ring with a nitro group, where will the new substituent be located?

13. If you add a second substituent to a benzene ring with an nitro group, will that reaction be faster or slower than adding a substituent to the benzene molecule with no substituents?

14. What characteristic does the nitro group have that dictates your answers to the above questions?

Now we will consider the chlorination of bromobenzene.



15. Which two of the above mechanisms are similar, and what do they have in common?

16. If you add a second substituent to a benzene ring with a halogen, where will the new substituent be located?

17. If you add a second substituent to a benzene ring with a halogen, will that reaction be faster or slower than adding a substituent to the benzene molecule with no substituents? Consider the positive charge on a halogen.

18. Substituents that speed up the rate of electrophilic aromatic substitution are called **activators**. Substituents that slow down the rate of electrophilic aromatic substitution are called **deactivators**. Classify each of the following substituents.

	Activator	Deactivator
Alkyl Groups		
Alkoxy Groups		
Nitro Groups		
Halogens		

19. Substituents that force an incoming electrophile to the ortho- and para-positions are called **ortho-, para-directors** and substituents that force an incoming electrophile to the meta-position are called **meta-directors**. Classify each of the following substituents.

	o-, p-director	m-director
Alkyl Groups		
Alkoxy Groups		
Nitro Groups		
Halogens		

41: DETERMINING THE DIRECTING EFFECT OF A SUBSTITUENT

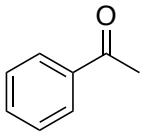
1. Why are alkyl groups activating / ortho-, para-directing?

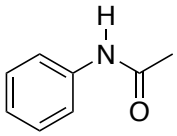
2. Why are alkoxy groups activating / ortho-, para-directing? (Don't just say "they have a 4th resonance structure" - what is it about the structure of the alkoxy group that allows for the 4th resonance structure?)

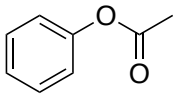
3. Explain why the nitro group is a deactivating meta-director. (Again, give your explanation in terms of the structure of the nitro group.)

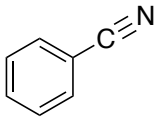
4. Explain why halogens are deactivators / ortho-, para-directors.

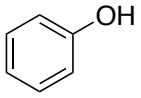
5. Classify each substituted benzene ring as activated or deactivated and as ortho-, para-directing or meta-directing.

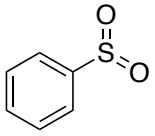




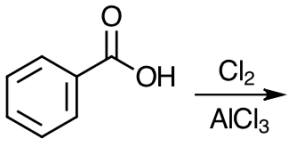


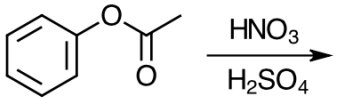


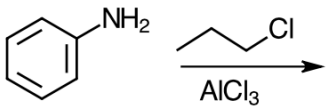




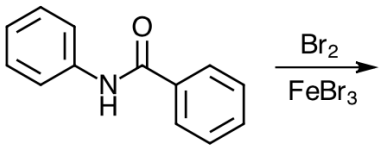
6. Predict the products of the following reactions. Some reaction will have more than one major product. Don't forget about the problems associated with Friedel-Crafts.







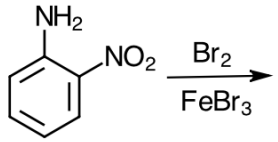
7. When you have more than one option of where to place an electrophile, consider the difference between activators and deactivators. The more thermodynamically-favorable reaction will occur.



42: MULTIPLE SUBSTITUENTS AND SYNTHESIS STRATEGIES

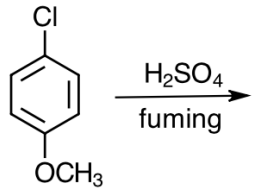
1. When you have more than one substituent on benzene, they can work together to direct the location of an incoming electrophile. Consider the following example, and:

   - Mark the carbon atom(s) where the NH_2 group will direct an electrophile.
   - Mark the carbon atom(s) where the NO_2 group will direct an electrophile.
   - Draw the major product(s) of the reaction.

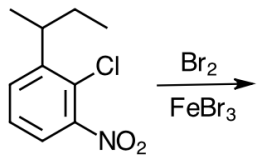


2. Sometimes, multiple substituents compete with each other to direct the location of an incoming electrophile. Consider the following example, and:

   - Mark the carbon atoms where the Cl will direct an electrophile.
   - Mark the carbon atoms where the OCH_3 will direct an electrophile.
   - Consider which substituent will control the reaction - which is the activator?
   - Draw the major product of the reaction.



3. Here is another example of competing substituents. Predict both products. Use steric hinderance to predict which will be the major product.



4. Start with benzene and use any reagents necessary to synthesize the following molecules. Before starting, take note of the following:

   - -NH_2 groups cannot be subjected to HNO_3/H_2SO_4 (the reagents for nitration). These reagents will destroy the -NH_2 group.
   - Friedel-Crafts reactions are thermodynamically unfavorable and cannot be done on a benzene ring that has any deactivating substituents already present.